Inside the Issue: Exploring the Current and Future Management of High-Risk, Hormone-Sensitive Nonmetastatic Prostate Cancer

A CME/MOC-Accredited Live Webinar

Monday, July 31, 2023
5:00 PM – 6:00 PM ET

Faculty

Neal D Shore, MD
Mary-Ellen Taplin, MD

Moderator

Neil Love, MD

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Faculty

Neal D Shore, MD
Medical Director
Carolina Urologic Research Center
Myrtle Beach, South Carolina

Mary-Ellen Taplin, MD
Professor of Medicine
Harvard School of Medicine
Dana-Farber Cancer Institute
Boston, Massachusetts

Moderator
Neil Love, MD
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Dr Love — Disclosures

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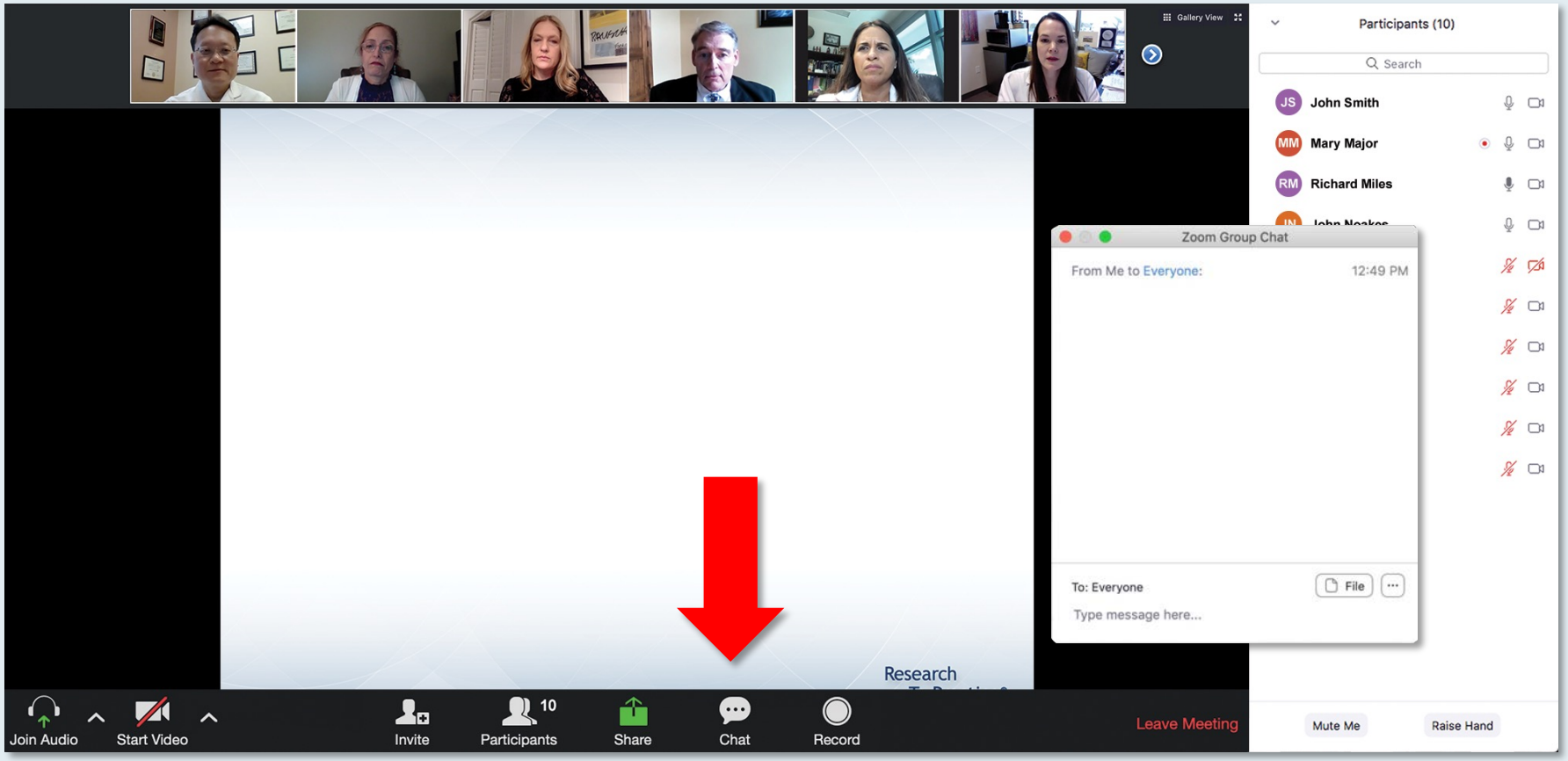

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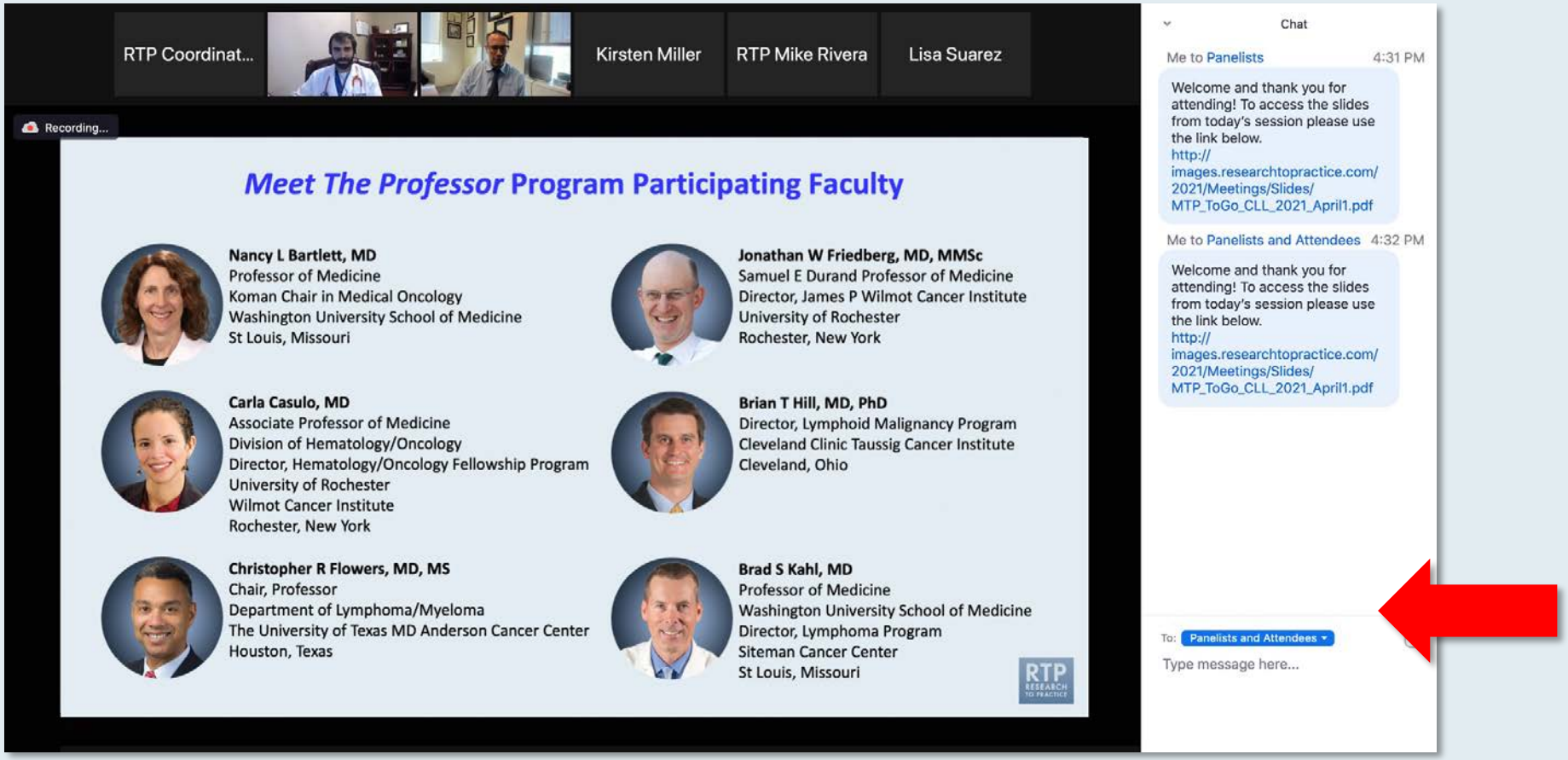

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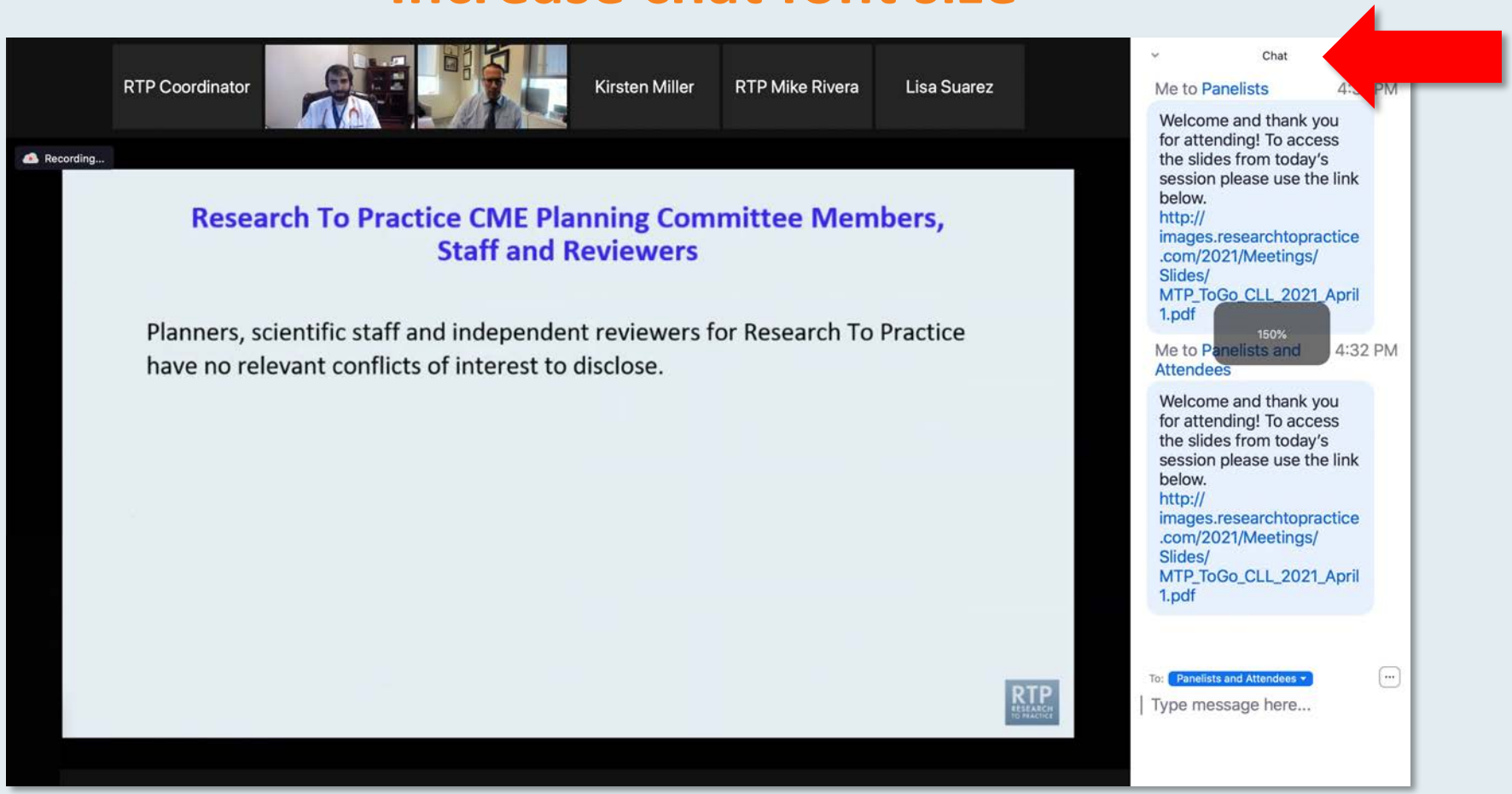

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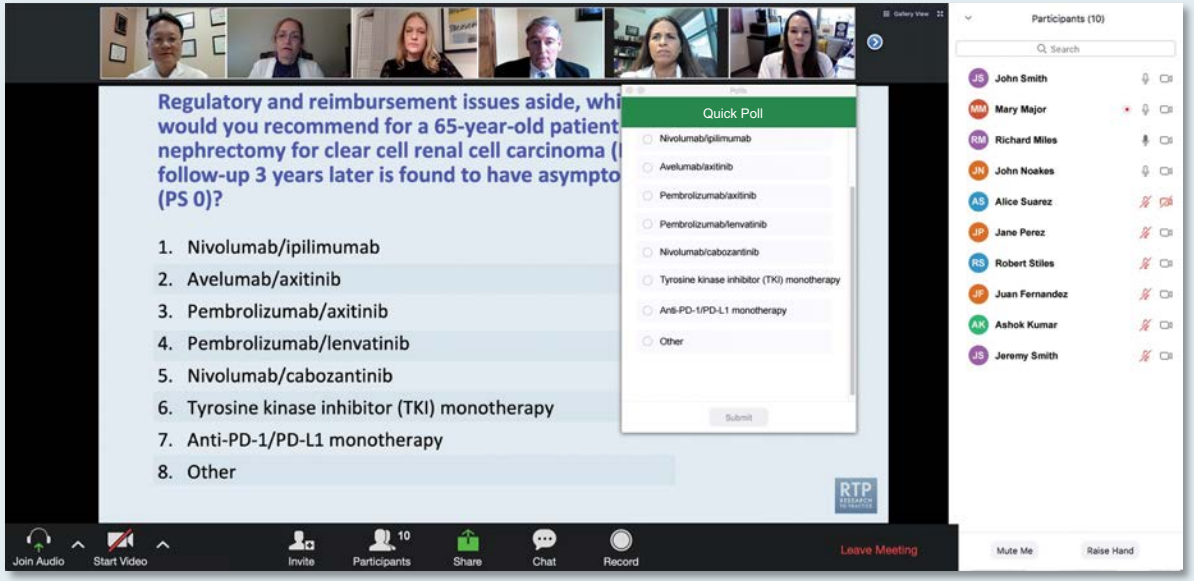

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Novel Agents and Strategies for the Treatment of Metastatic Castration-Resistant Prostate Cancer

DR EVAN YU

FRED HUTCHINSON CANCER RESEARCH CENTER

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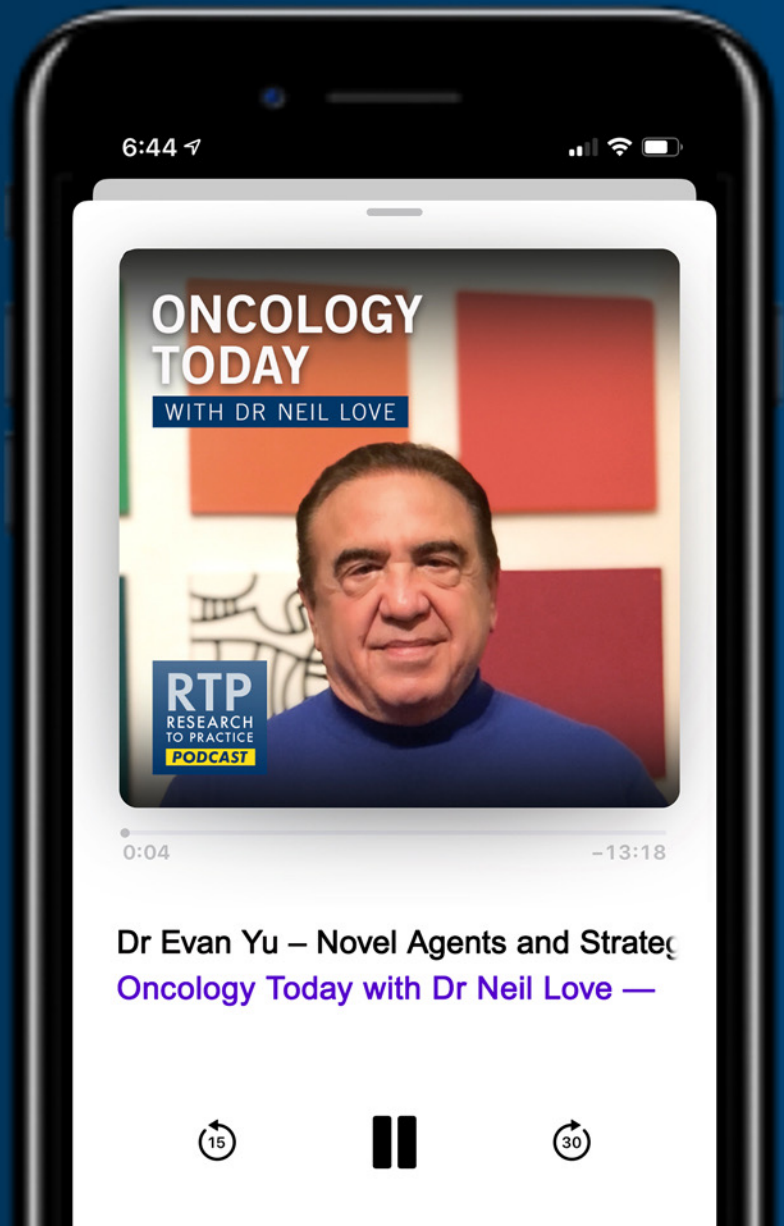

Inside the Issue: The Current and Future Role of CD20 x CD3 Bispecific Antibodies in the Management of Non-Hodgkin Lymphoma

A CME/MOC-Accredited Live Webinar

Wednesday, August 2, 2023
5:00 PM – 6:00 PM ET

Faculty

Martin Hutchings, MD, PhD
Loretta J Nastoupil, MD

Moderator

Neil Love, MD

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Inside the Issue: Optimizing the Management of Metastatic Pancreatic Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, August 8, 2023
5:00 PM – 6:00 PM ET

Faculty

Eileen M O'Reilly, MD
Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Melanoma

Thursday, August 10, 2023
5:00 PM – 6:00 PM ET

Faculty

Prof Georgina Long, AO, BSc, PhD, MBBS

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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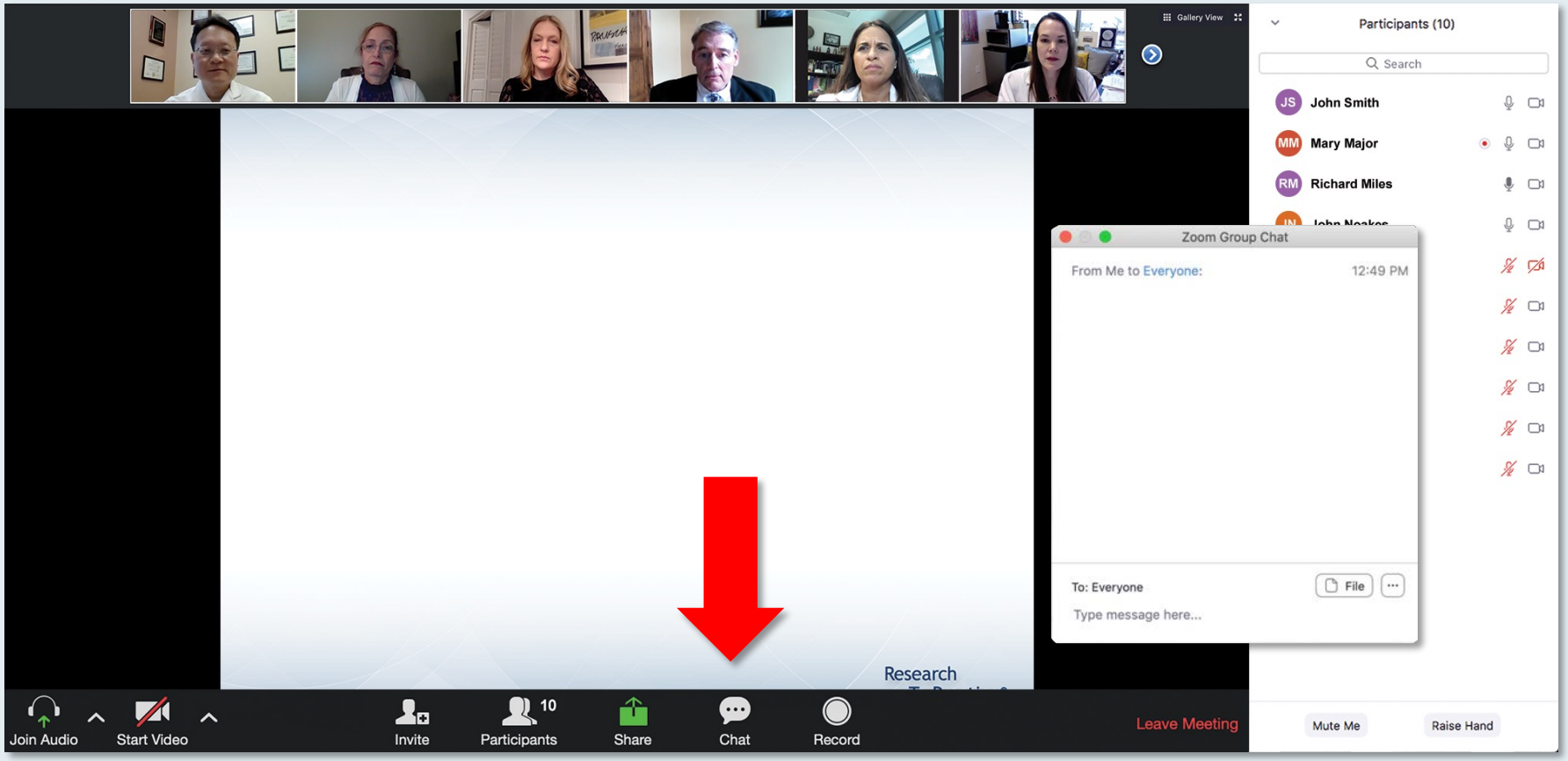

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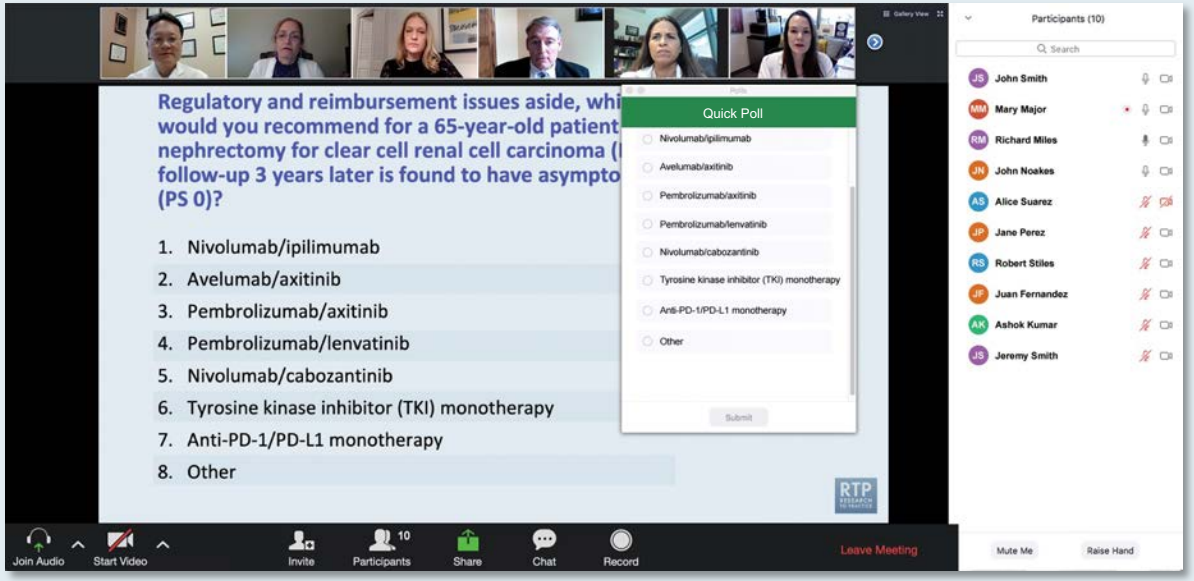

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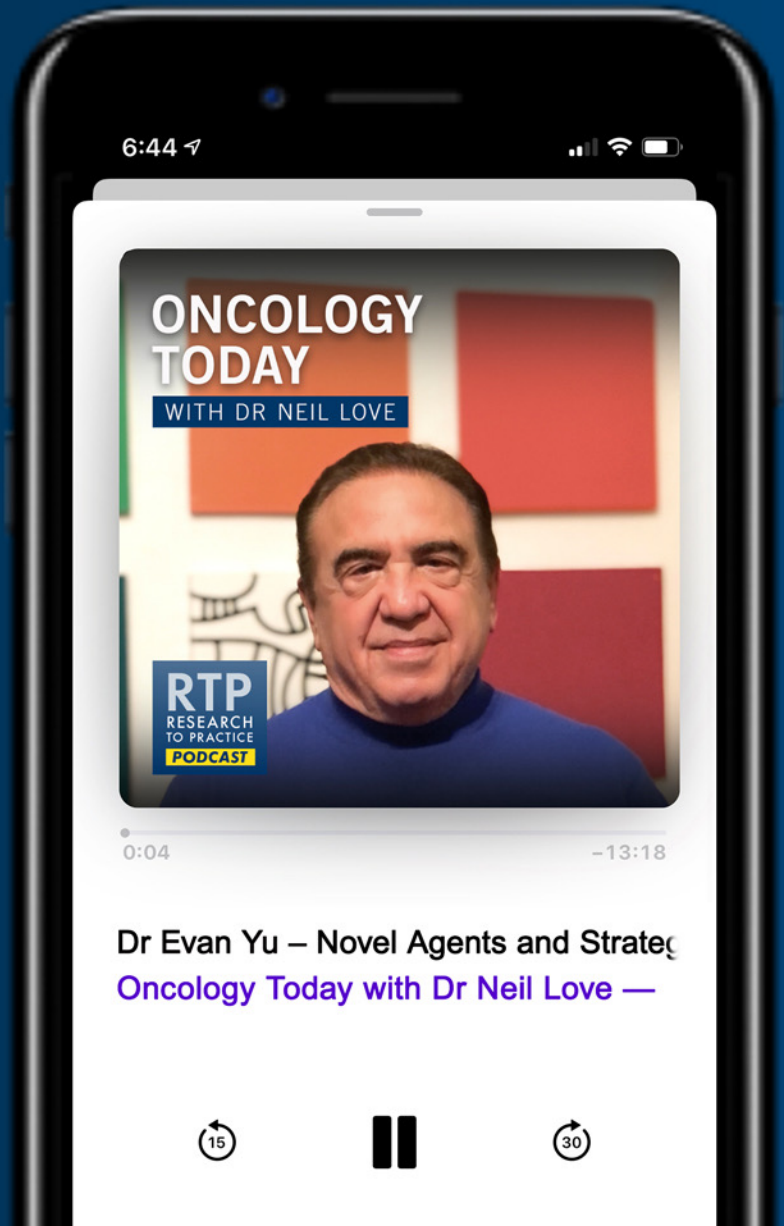

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Treatment Intensification for Locally Advanced and BCR Prostate Cancer Patients

Neal Shore, MD, FACS

Key Data Sets

Neal D Shore, MD

- Aggarwal R et al. PRESTO: A phase 3 open-label study of androgen annihilation in patients with high-risk biochemically relapsed prostate cancer (AFT-19). ESMO 2022;Abstract LBA63.
- ATLAS: A randomized, double-blind, placebo-controlled phase 3 study of [apalutamide] in subjects with high-risk, localized or locally advanced prostate cancer receiving treatment with primary radiation therapy. (NCT02531516)
- Attard G et al. Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: A meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol. *Lancet* 2022 January 29;399(10323):447-60.
- Bolla M et al. Long-term results with immediate androgen suppression and external irradiation in patients with locally advanced prostate cancer (an EORTC study): A phase III randomised trial. *Lancet* 2002;360(9327):103-6.
- ENZARAD: Randomised phase 3 trial of enzalutamide in androgen deprivation therapy with radiation therapy for high risk, clinically localised, prostate cancer. (NCT02446444)

Key Data Sets

Neal D Shore, MD (continued)

- Nabid A et al. Duration of androgen deprivation therapy in high-risk prostate cancer: A randomized phase III trial. *Eur Urol* 2018;74(4):432-41.
- Polkinghorn WR et al. Androgen receptor signaling regulates DNA repair in prostate cancers. *Cancer Discov* 2013;3(11):1245-53.
- PEACE-2: A randomized phase III, factorial design, of cabazitaxel and pelvic radiotherapy in patients with localized prostate cancer and high-risk features of relapse. (NCT01952223)
- Shore ND et al. EMBARK: A phase 3 randomized study of enzalutamide or placebo plus leuprolide acetate and enzalutamide monotherapy in high-risk biochemically recurrent prostate cancer. AUA 2023;Abstract LBA02-09.

Agenda

INTRODUCTION: Interdisciplinary Management of Prostate Cancer

MODULE 1: Key Data Sets

MODULE 2: Faculty Survey

MODULE 3: Faculty Cases

Appendix

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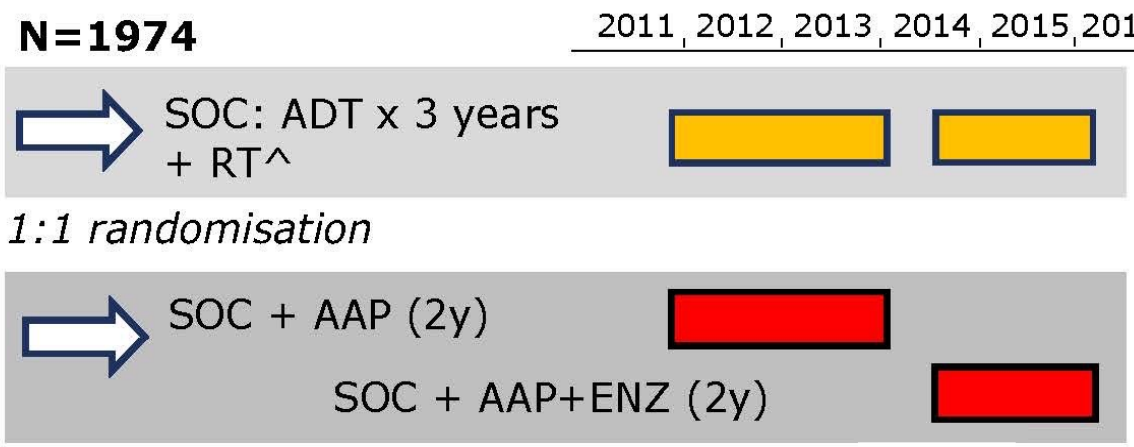
Treatment Intensification for Locally Advanced and BCR Prostate Cancer Patients

Neal Shore, MD, FACS

STAMPEDE: Abiraterone ± Enzalutamide in nmCSPC

Study design

- M0 pts in AAP comparison: continued FU with **no further** efficacy inspections
- 2019 - amended the reporting plan* to split M1 & M0, power the 1^{ary} end-point on MFS, meta-analyse with new data from AAP+ENZ comparison



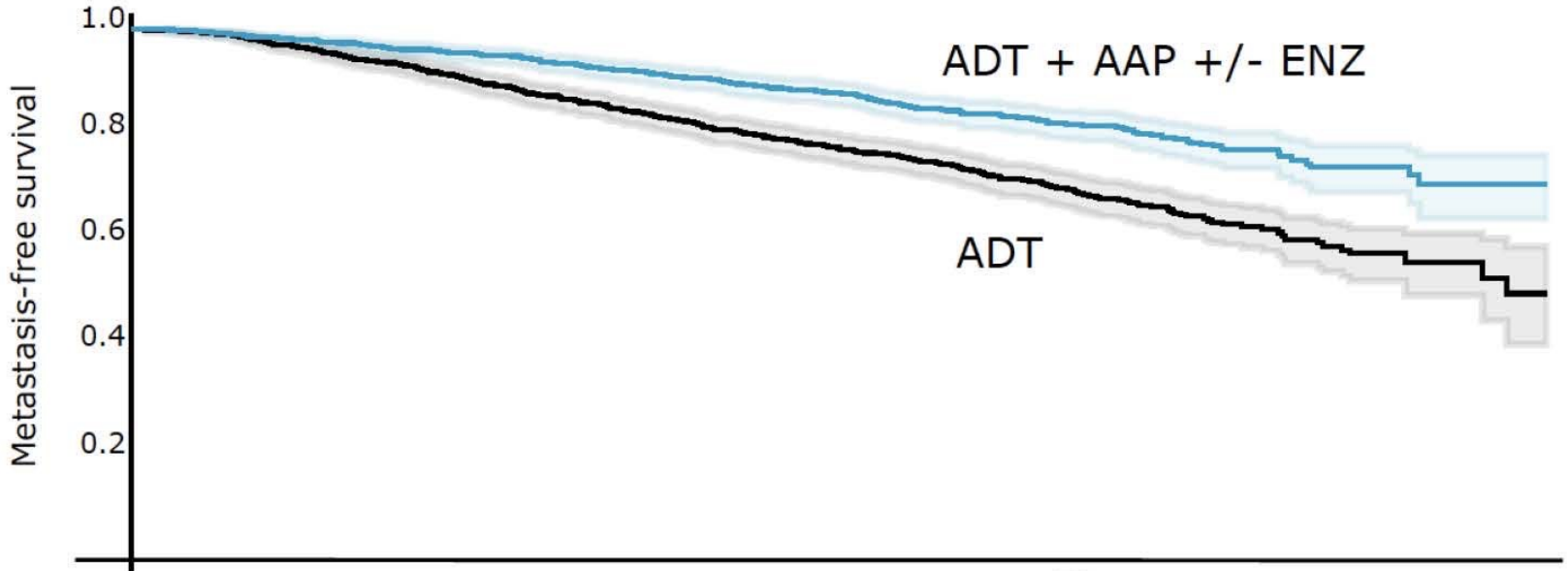
- No overlapping controls
- Same protocol & eligibility criteria
- 2 years AAP+/-ENZ
- No evidence of OS benefit with AAP+/-ENZ in mCRPC [1]

Courtesy of Neal D Shore, MD

Attard, et al. Lancet, 2022

STAMPEDE: Abiraterone ± Enzalutamide in nmCSPC

Metastasis-free survival



ADT										
At-risk	988	950	894	836	767	550	329	172	53	9
Censored	0	8	11	14	26	201	387	522	632	673
Event	0	30	83	138	195	237	272	294	303	306
ADT+AAP+/-ENZ										
At-risk	986	948	917	884	839	622	369	198	71	14
Censored	0	21	28	31	45	225	460	615	737	792
Event	0	17	41	71	102	139	157	173	178	180

Events
180 ADT+ AAP +/- ENZ
306 ADT

HR:	**0.53**
95% CI:	0.44-0.64
P value	2.9×10^{-11}

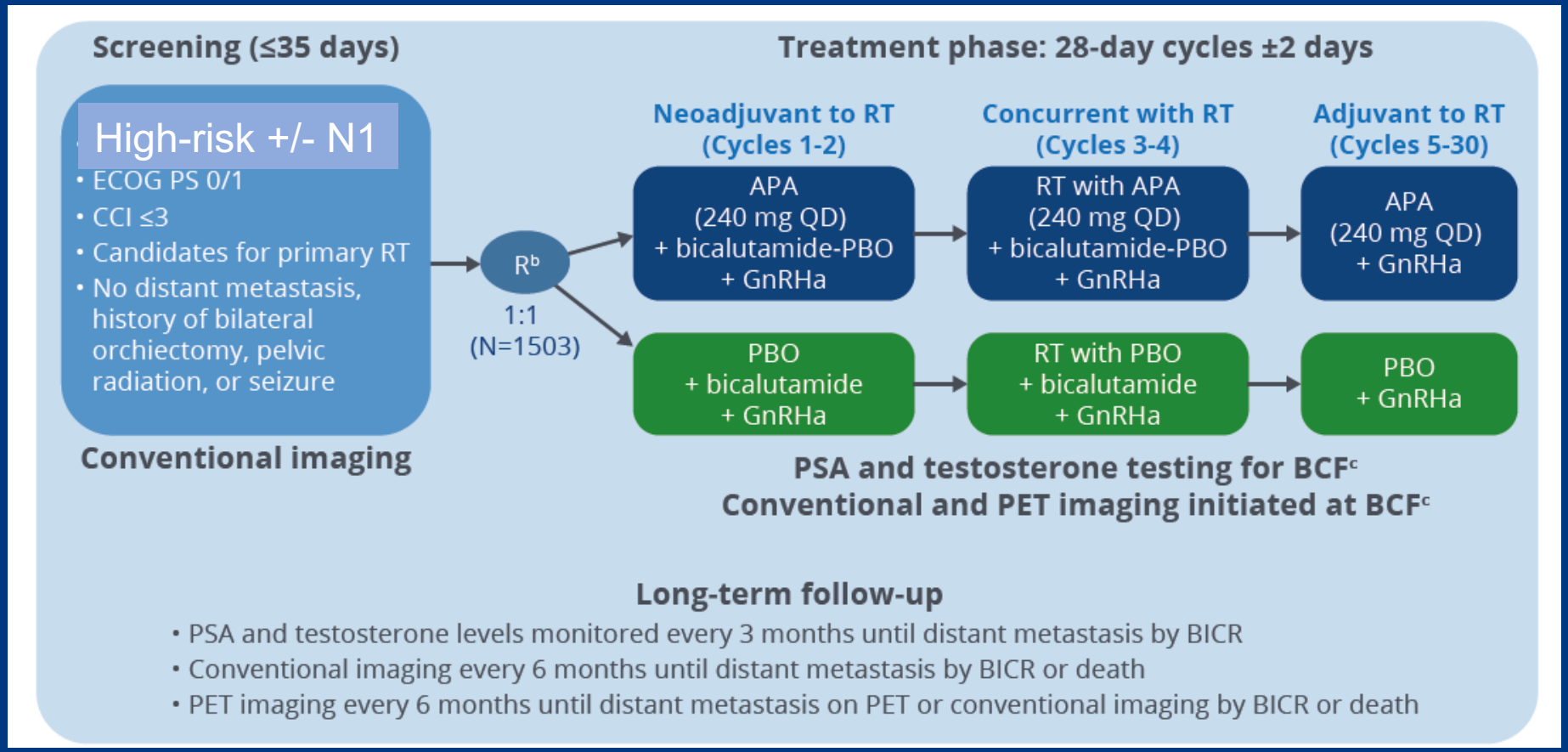
6-year MFS improved from 69% to 82%

Courtesy of Neal D Shore, MD

Attard, et al. Lancet, 2022

ATLAS trial design

N1=13%



MFS

Courtesy of Neal D Shore, MD

ENZARAD (ANZUP 1303) STUDY SCHEMA

Study Chairs:
Scott Williams & Paul Nguyen

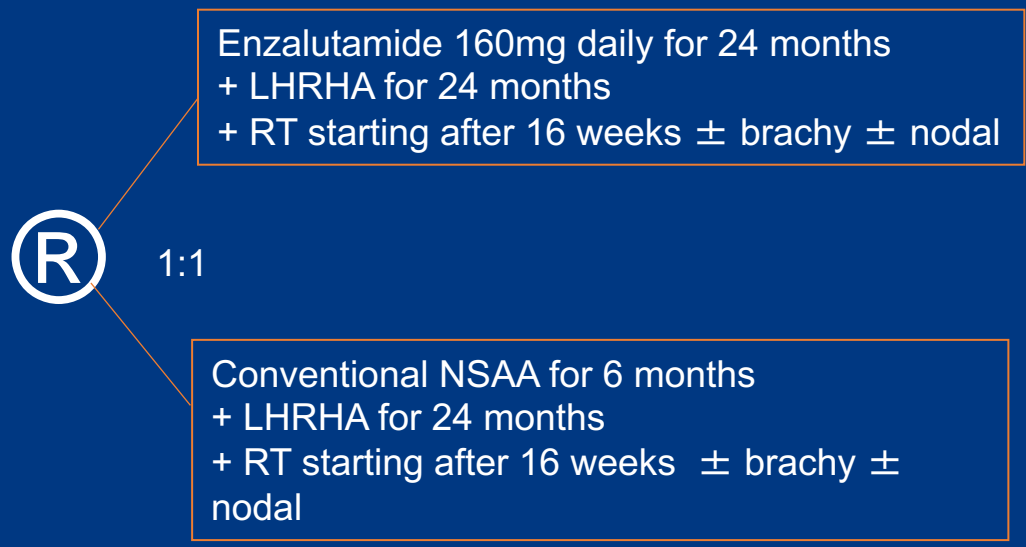
n= 802 participants

Eligibility

Localized prostate cancer
High risk of recurrence
Suitable for EBRT

Stratification

Gleason score 8-10
T3-4 disease
N1 disease
PSA ≥20 ng/mL
Brachytherapy boost
Pelvic nodal RT
Study Site



Endpoints

Metastasis-free survival (primary)
Overall survival
Cause specific survival
PSA progression free survival
Clinical progression free survival
Castration-resistance
Health related quality of life
Adverse events
Incremental cost-effectiveness

*Conventional Non-Steroidal Anti-Androgens: bicalutamide 50mg daily, nilutamide 150mg daily, or flutamide 250mg tid

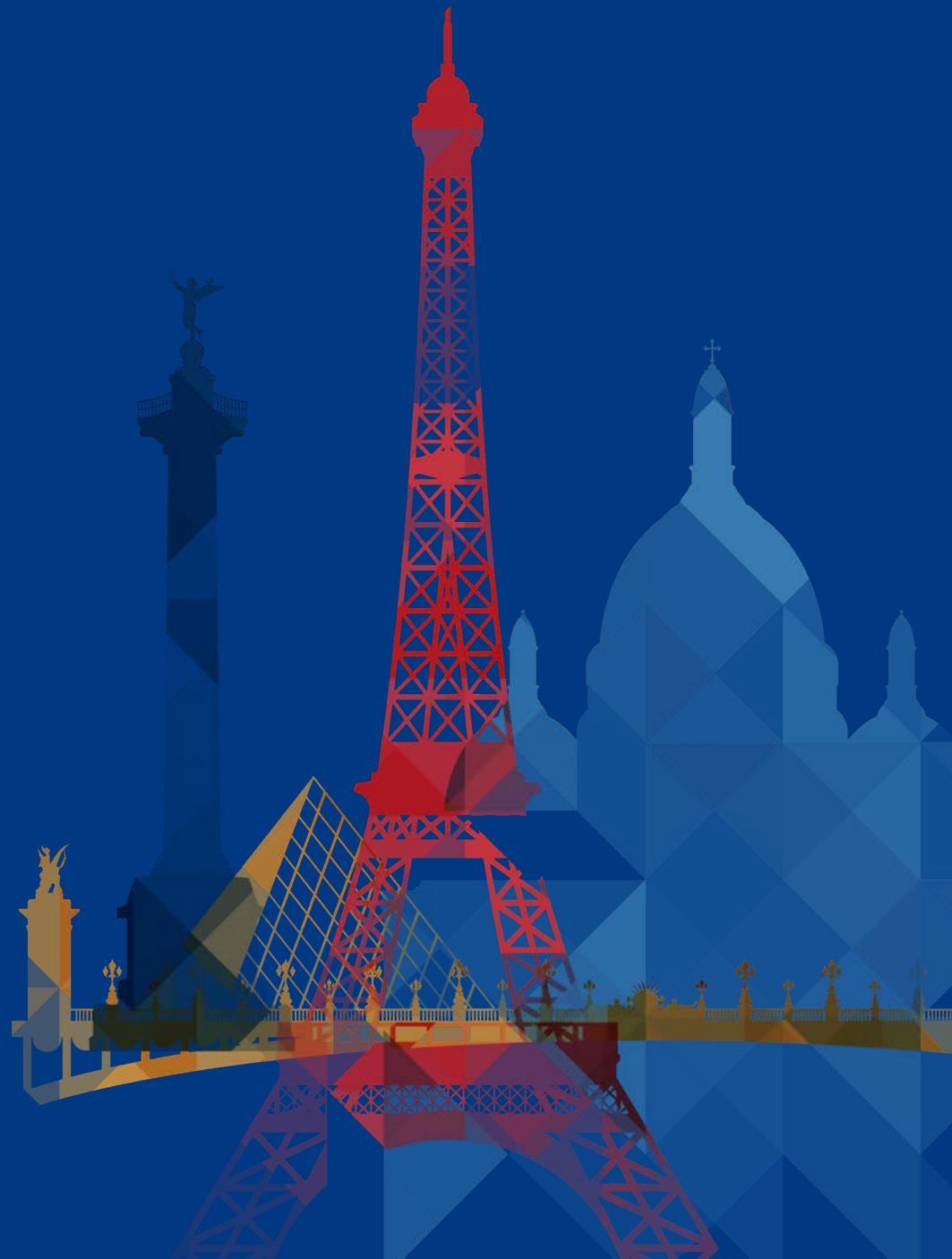
Courtesy of Neal D Shore, MD

PARIS 2022 ESMO congress

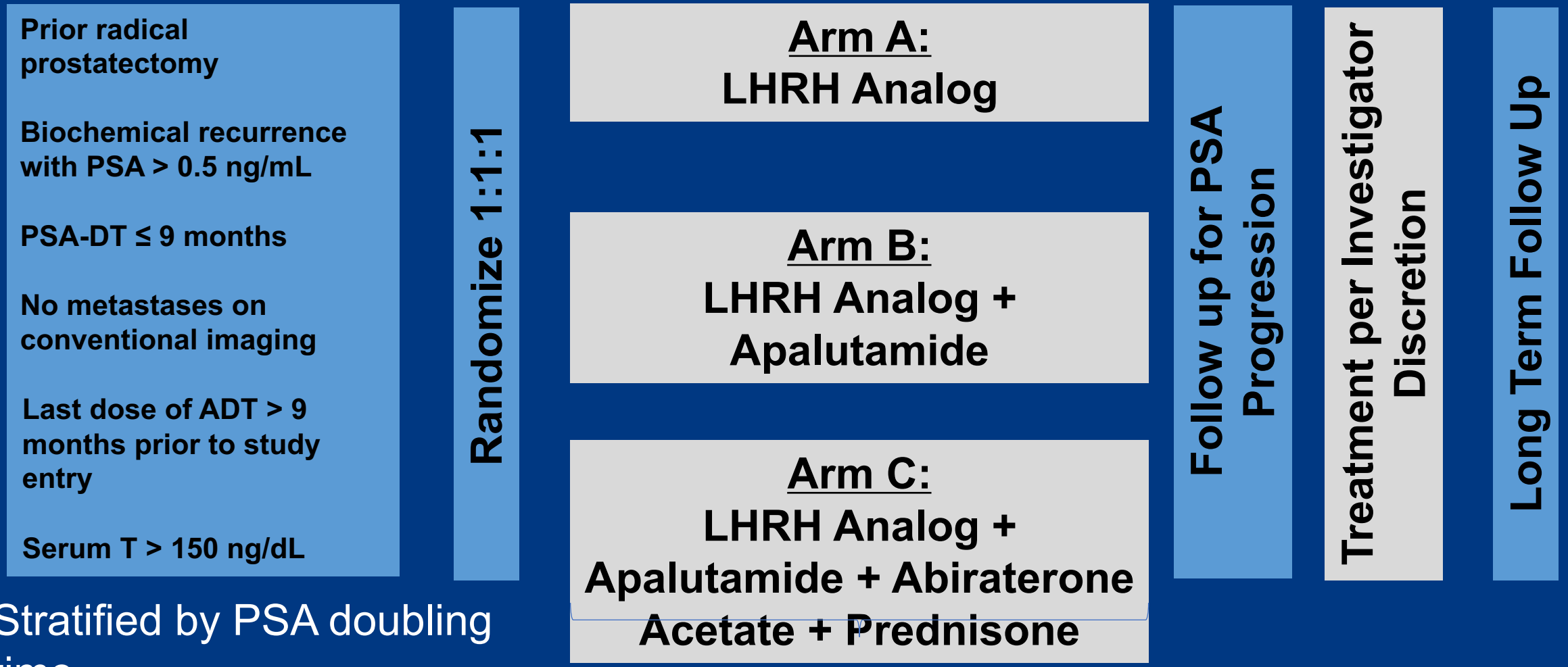
PRESTO: A Phase 3 Open-Label Study of Androgen Annihilation in Patients with High-Risk Biochemically Relapsed Prostate Cancer (AFT-19)

Rahul Aggarwal, on behalf of the Alliance AFT-19 Study Investigators

Paris, France
11 SEP 2022



Study Schema



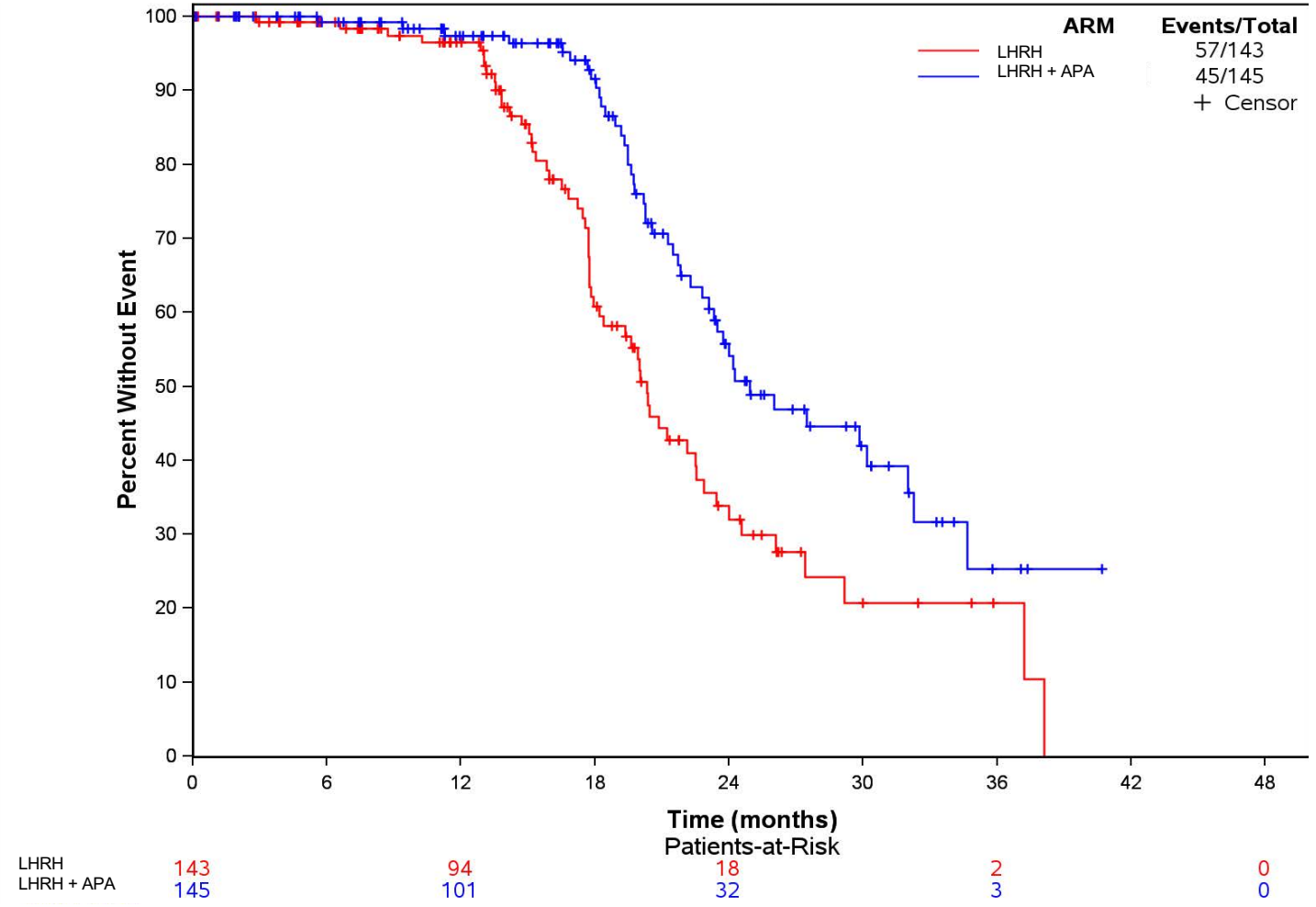
Stratified by PSA doubling time
(< 3 months vs. 3 – 9 months)

52 Weeks

Courtesy of Neal D Shore, MD

Aggarwal R et al. ESMO 2022;Abstract LBA63.

Arm B: ADT + apalutamide vs. ADT monotherapy

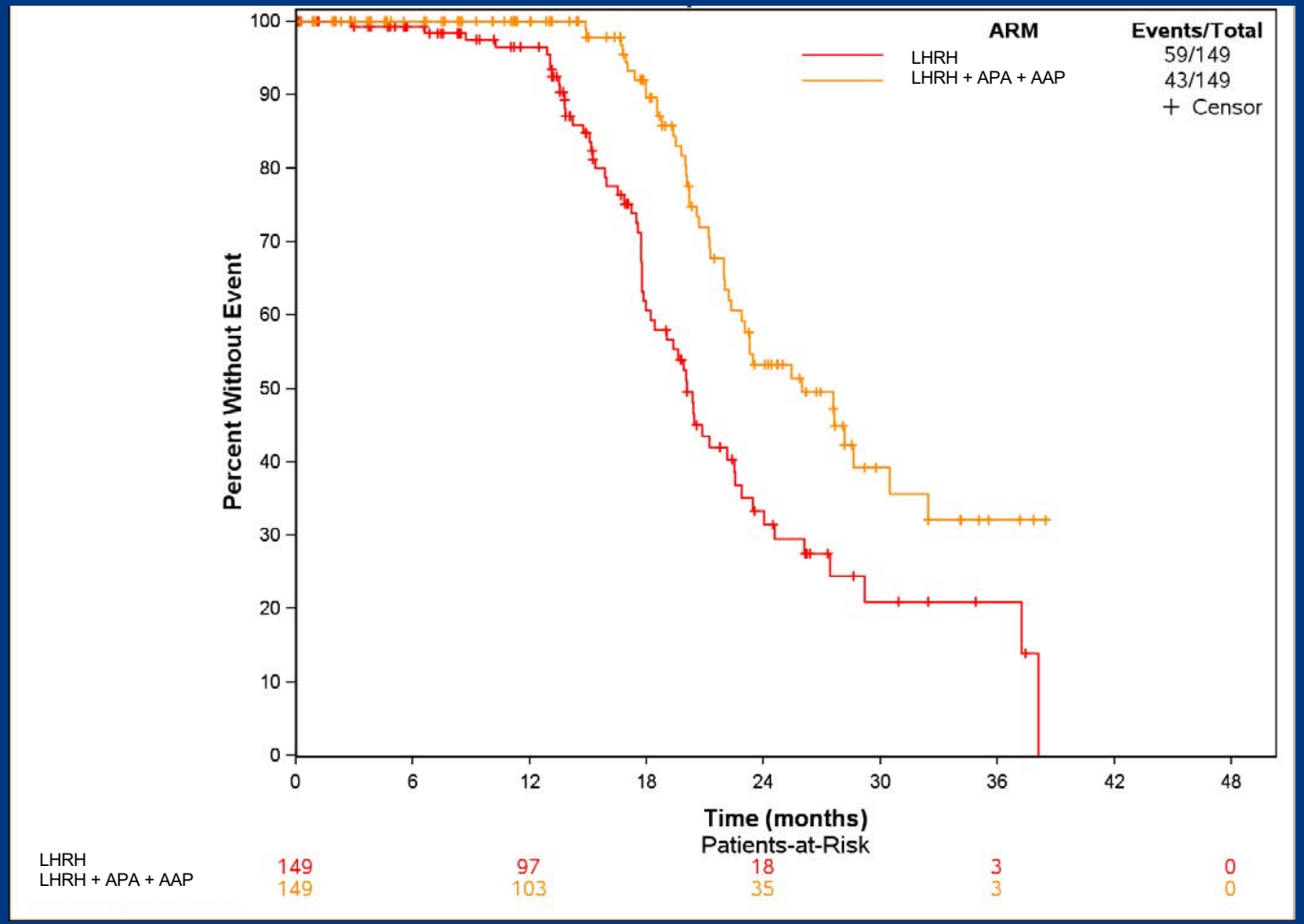


- Median follow up 21.5 months
- 102 PSA PFS events
- Median PSA progression-free survival
  - ADT + APA = 24.9 months (95% CI: 23.3 – 32.3)
  - ADT alone = 20.3 months (95% CI: 18.2 – 22.9)
  - **Hazard ratio 0.52 (95% CI: 0.35 – 0.77)**
  - One-sided p-value = 0.00047)

Courtesy of Neal D Shore, MD

Aggarwal R et al. ESMO 2022;Abstract LBA63.

Arm C: ADT + apalutamide + abiraterone acetate + prednisone vs. ADT monotherapy



- Median follow up 21.3 months
- 102 PSA PFS events
- Median PSA progression-free survival
  - ADT + APA + AAP = 26.0 months (95% CI: 22.9 – 32.5)
  - ADT alone = 20.0 months (95% CI: 18.2 – 22.5)
  - **Hazard ratio = 0.48 (95% CI: 0.32 – 0.71)**
  - One-sided p-value = 0.00008

Courtesy of Neal D Shore, MD

Aggarwal R et al. ESMO 2022;Abstract LBA63.

Most Common Grade ≥ 2 Adverse Events (N = 484)

	Arm A (n = 160)		Arm B (n = 163)		Arm C (n = 161)	
Adverse Events (AE)	Grade 2	Grade ≥ 3	Grade 2	Grade ≥ 3	Grade 2	Grade ≥ 3
	n (%)		n (%)		n (%)	
Hypertension	19 (12)	12 (8)	25 (15)	12 (7)	18 (11)	31 (19)
Hot flashes	19 (12)	1 (1)	8 (5)	0	23 (14)	0
Fatigue	14 (9)	0	8 (5)	3 (2)	16 (10)	2 (1)
Injection site reaction	9 (6)	0	10 (6)	0	11 (7)	0
Insomnia	9 (6)	0	5 (3)	0	8 (5)	0
Hyperglycemia	0	3 (2)	6 (4)	2 (1)	6 (4)	5 (3)
Rash	2 (1)	1 (1)	7 (4)	3 (2)	3 (2)	5 (3)
Erectile dysfunction	10 (6)	1 (1)	6 (4)	1 (1)	2 (1)	0
Arthralgia	4 (3)	1 (1)	6 (4)	1 (1)	3 (2)	2 (1)
Elevated ALT	1 (1)	0	1 (1)	0	2 (1)	0

Courtesy of Neal D Shore, MD

Aggarwal R et al. ESMO 2022;Abstract LBA63.

Summary of Adverse Events (N = 484)

	Arm A (n=160)	Arm B (n=163)	Arm C (n=161)
Adverse Events (AE)	n (%)	n (%)	n (%)
Any AE	145 (90.6)	148 (90.8)	155 (96.3)
Grade 3 or 4 AE	30 (18.8)	41 (25.2)	61 (37.9)
Any Serious AE	13 (8.1)	14 (8.6)	28 (17.4)
AE leading to treatment discontinuation	0 (0.0)	3 (1.8)	5 (3.1)

Courtesy of Neal D Shore, MD

Aggarwal R et al. ESMO 2022;Abstract LBA63.

Limitations

- PSA-based rather than metastasis-free survival primary endpoint
  - Follow up is ongoing to estimate median metastasis-free survival in each study arm

- Metabolic imaging (e.g. fluciclovine or PSMA PET) not required at screening
  - Truly M0 biochemically recurrent CSPC population shrinking with stage migration
  - Role of metastasis-directed therapy in oligometastatic CSPC in conjunction with ADT remains to be defined

Courtesy of Neal D Shore, MD

Aggarwal R et al. ESMO 2022;Abstract LBA63.

Conclusions

- PRESTO is the first phase 3 study to report results of ADT plus AR pathway inhibition in biochemically recurrent, non-metastatic, castration-sensitive prostate cancer

- The addition of apalutamide to androgen deprivation for a finite duration of treatment leads to a statistically significant prolongation of PSA progression-free survival
  - No adverse impact on time to testosterone recovery
  - Safety profile consistent with prior studies

- There does not appear to be further benefit with addition of abiraterone acetate + prednisone to apalutamide

Courtesy of Neal D Shore, MD

Aggarwal R et al. ESMO 2022;Abstract LBA63.

Conclusions (continued)

- Follow up is ongoing to estimate the impact of ADT plus AR pathway inhibition on patient-reported outcomes, time to subsequent therapy, and metastasis-free survival

- Given that treatment decisions in biochemically recurrent prostate cancer are often predicated on PSA kinetics alone, ADT plus apalutamide for a finite treatment period could be considered for high-risk patients with a short PSA doubling time

Courtesy of Neal D Shore, MD

Aggarwal R et al. ESMO 2022;Abstract LBA63.

Depth of PSA Nadir and Subsequent PSA Progression-Free Survival in Patients (pts) with High-Risk Biochemically Relapsed Prostate Cancer: Results from the Phase 3 PRESTO Study (AFT-19)

Aggarwal RR et al

ASCO 2023;Abstract 5077.

A Prospective Trial of Apalutamide and Abiraterone Acetate plus Prednisone in Black and White Men with Metastatic Castrate-Resistant Prostate Cancer

George DJ et al

ASCO 2023;Abstract 5015.

EMBARK study design

Patient population:

- Screening PSA ≥1 ng/mL after RP and at least 2 ng/mL above the nadir for primary EBRT
- PSADT ≤9 mo
- No metastases on bone scan or CT/MRI per central read
- Testosterone ≥150 ng/dL
- Prior hormonal therapy ≥9 mo prior to R (neoadjuvant/adjuvant for ≤36 mo OR ≤6 mo for rising PSA)

Stratification factors:

- Screening PSA (≤10 ng/mL vs. >10 ng/mL)
- PSADT (≤3 mo vs. >3 to ≤9 mo)
- Prior hormonal therapy (yes vs. no)

R
1:1:1

N = 1068

Enzalutamide (160 mg oral qd) + leuprolide acetate (22.5 mg IM/q12w)
n = 355
Blinded

Placebo + leuprolide acetate (22.5 mg IM/q12w)
n = 358
Blinded

Enzalutamide monotherapy (160 mg oral qd)
n = 355
Unblinded

PSA <0.2 ng/mL at week 36

Yes → Suspend treatment at week 37 Monitor PSA (reinitiate if PSA rises)[a]

No → Remain on treatment

Primary endpoint[b]:
MFS by BICR, enzalutamide + leuprolide acetate vs. leuprolide acetate alone

Key secondary endpoints[b,c]:

- MFS by BICR, enzalutamide monotherapy vs. leuprolide acetate alone
- Time to PSA progression
- Time to first use of new antineoplastic therapy
- OS[c]

Other secondary endpoints:

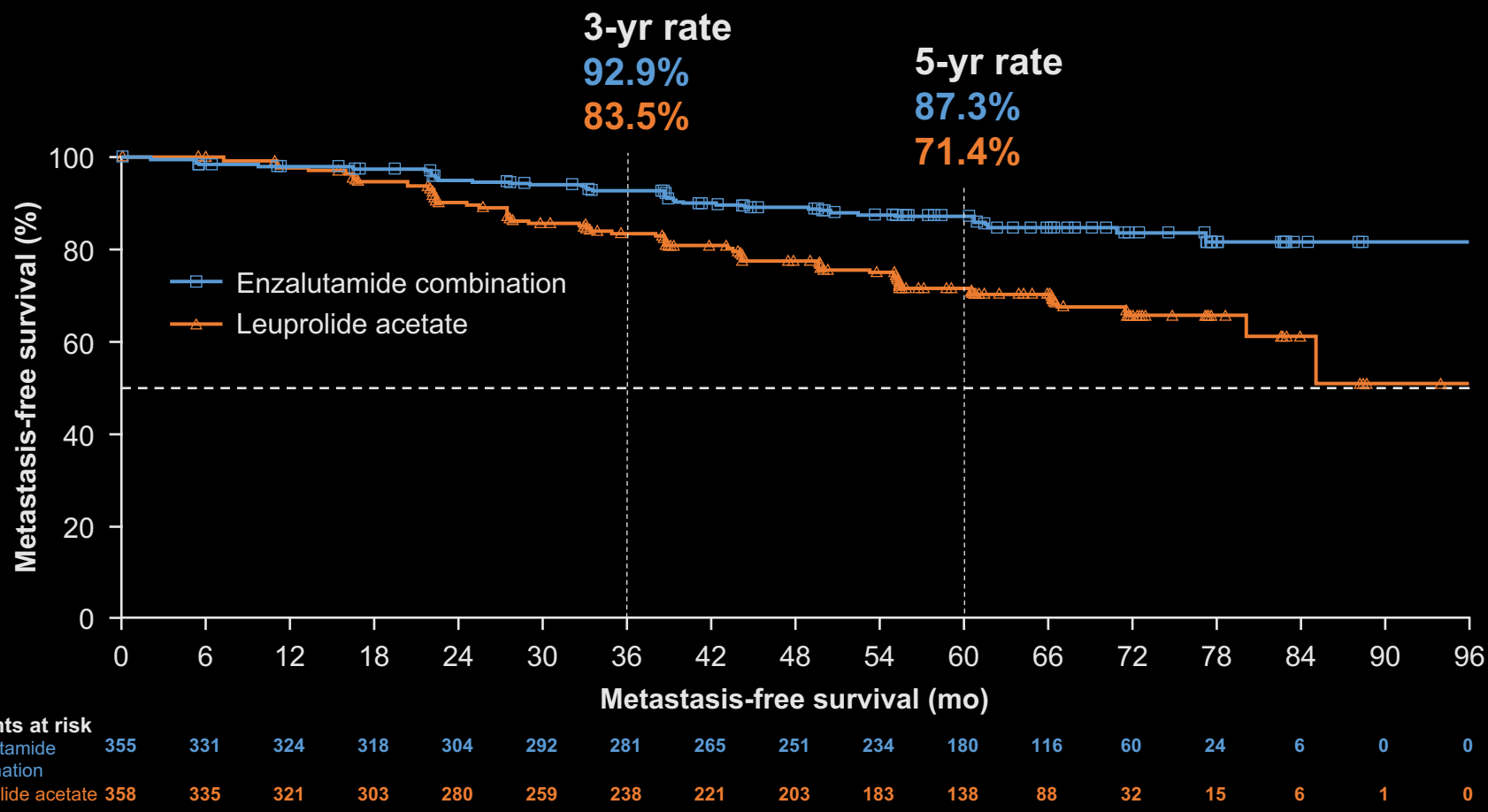
- Safety[d]

[a]Study treatment was suspended once at week 37 if PSA was <0.2 ng/mL and restarted when PSA was ≥5.0 ng/mL (without prior RP) and ≥2 ng/mL (prior RP). [b]Intent-to-treat population. [c]Primary endpoint and key secondary endpoints for enzalutamide combination and enzalutamide monotherapy are alpha-protected. *P*-value to determine significance for OS of combination and monotherapy treatment comparisons was dependent on outcomes of primary endpoint and key secondary endpoints. [d]Safety population. BICR, blinded independent central review; CT, computed tomography; d, day; EBRT, external beam radiotherapy; IM, intramuscular; MFS, metastasis-free survival; mo, month; MRI, magnetic resonance imaging; OS, overall survival; PSA, prostate-specific antigen; PSADT, PSA doubling time; q, every; R, randomization; RP, radical prostatectomy; w, weeks.

Courtesy of Neal D Shore, MD

Shore N et al. AUA 2023;Abstract LBA02-09.

Primary endpoint — MFS for enzalutamide combination vs. leuprolide acetate



	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)
Median follow-up, mo	60.7	60.6
Events, n (%)	45 (13)	92 (26)
Per BICR, median MFS (95% CI), mo	NR (NR)	NR (85.1–NR)

HR (95% CI): 0.42 (0.31–0.61); *P*<0.0001[a]

A consistent treatment effect was seen for investigator-assessed MFS: HR (95% CI): 0.47 (0.37–0.67); *P*<0.0001

Data cutoff: January 31, 2023. Symbols indicate censored data. [a]HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide combination; the two-sided *P*-value was based on a stratified log-rank. CI, confidence interval; HR, hazard ratio; IWRS, interactive web response system; NR, not reached.

Courtesy of Neal D Shore, MD

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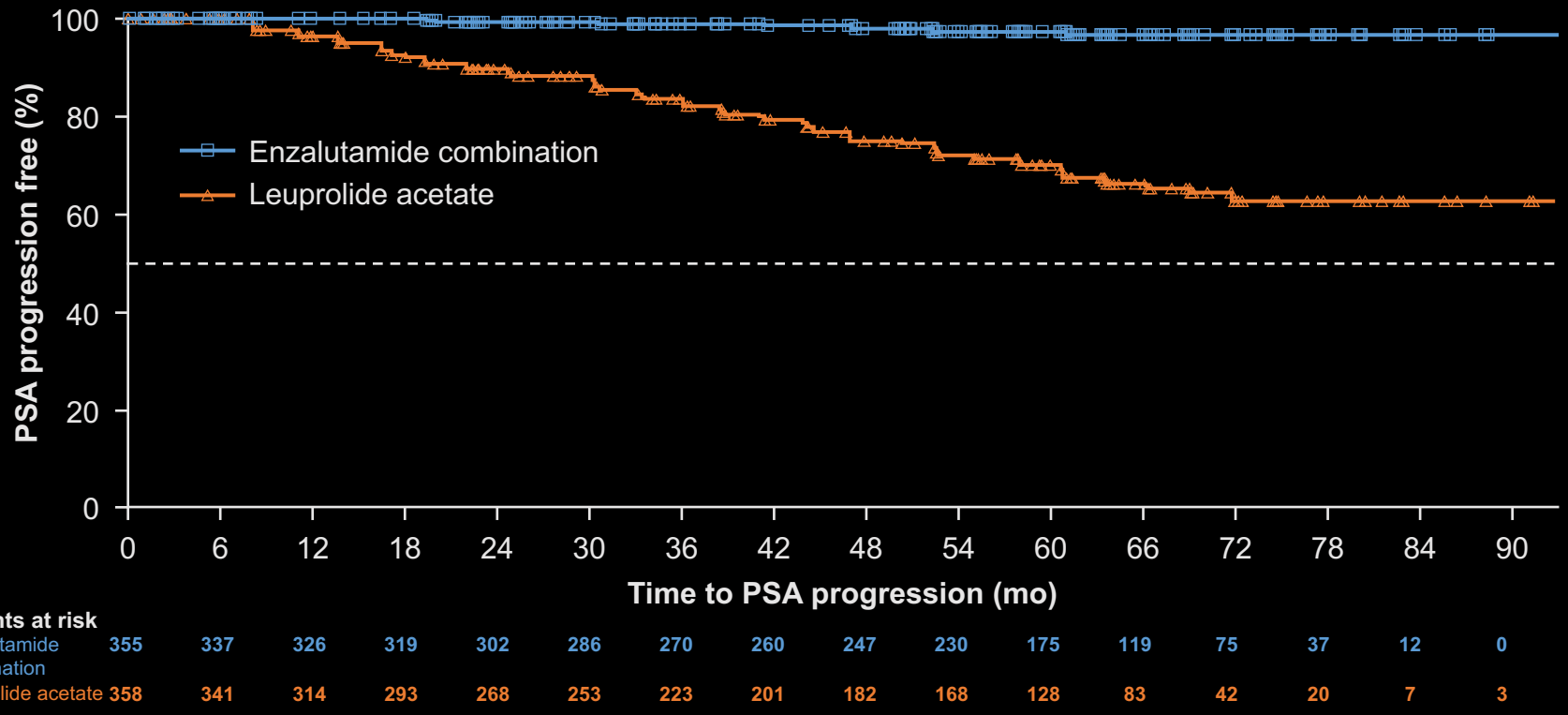
Key secondary endpoint — Time to PSA progression for enzalutamide combination vs. leuprolide acetate



	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)
Events, n (%)	8 (2)	93 (26)
Median time to PSA progression (95% CI), mo	NR (NR)	NR (NR)

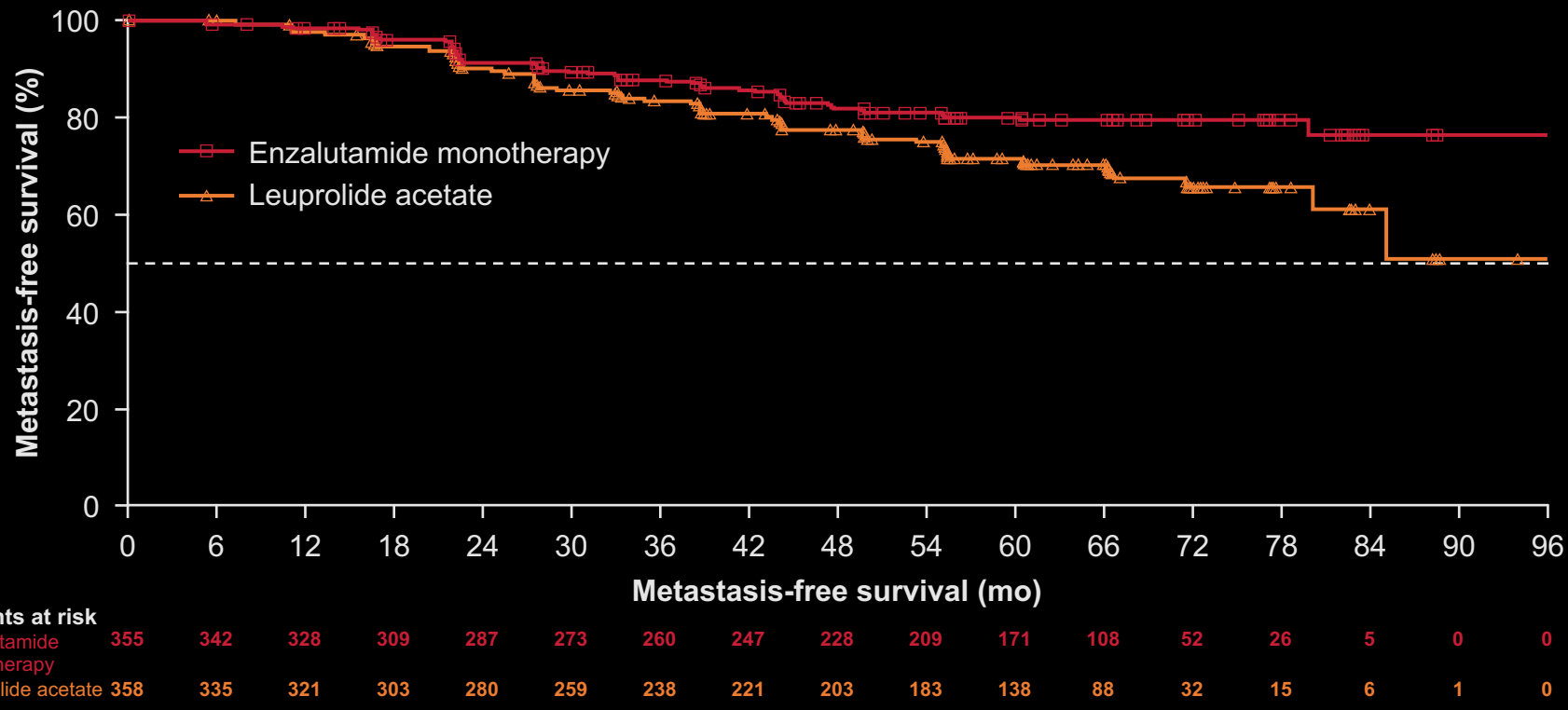
HR (95% CI): 0.07 (0.03–0.14); *P*<0.0001[a]

Data cutoff: January 31, 2023. Symbols indicate censored data. [a]The HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide combination; the two-sided *P*-value is based on a stratified log-rank test.

Courtesy of Neal D Shore, MD

Shore N et al. AUA 2023;Abstract LBA02-09.

Key secondary endpoint — MFS for enzalutamide monotherapy vs. leuprolide acetate



	Enzalutamide monotherapy (n = 355)	Leuprolide acetate (n = 358)
Median follow-up, mo	60.7	60.6
Events, n (%)	63 (18)	92 (26)
Per BICR, median MFS (95% CI), mo	NR (NR)	NR (85.1–NR)

HR (95% CI): 0.63 (0.46–0.87); *P*=0.0049[a]

A consistent treatment effect was seen for investigator-assessed MFS: HR (95% CI): 0.56 (0.40–0.78); *P*=0.0006

Data cutoff: January 31, 2023. Symbols indicate censored data. [a]The HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide monotherapy; the two-sided *P*-value was based on a stratified log-rank test.

Courtesy of Neal D Shore, MD

Shore N et al. AUA 2023;Abstract LBA02-09.

Safety profile

Event, n (%)[a]	Enzalutamide combination (n = 353)		Leuprolide acetate (n = 354)		Enzalutamide monotherapy (n = 354)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Any AE	343 (97.2)	164 (46.5)	345 (97.5)	151 (42.7)	347 (98.0)	177 (50.0)
Treatment-related AE	305 (86.4)	62 (17.6)	283 (79.9)	31 (8.8)	312 (88.1)	57 (16.1)
Serious AE	123 (34.8)	110 (31.2)	112 (31.6)	100 (28.2)	131 (37.0)	116 (32.8)
Treatment-related serious AE	26 (7.4)	22 (6.2)	8 (2.3)	7 (2.0)	17 (4.8)	17 (4.8)
AE leading to dose reduction	25 (7.1)	11 (3.1)	16 (4.5)	5 (1.4)	56 (15.8)	14 (4.0)
AE leading to permanent discontinuation	73 (20.7)	31 (8.8)	36 (10.2)	19 (5.4)	63 (17.8)	34 (9.6)
AE leading to death	6 (1.7)[b]	–	3 (0.8)[b]	–	8 (2.3)[b]	–

- Median treatment duration excluding treatment suspension was 32.4 mo (range, 0.1–83.4 mo) for enzalutamide combination, 35.4 mo (range, 0.7–85.7 mo) for leuprolide acetate, and 45.9 mo (0.4–88.9 mo) for enzalutamide monotherapy.
- The most common AE leading to study drug discontinuation was fatigue (enzalutamide combination, 3.4% [n = 12]; leuprolide acetate, 1.1% [n = 4]; enzalutamide monotherapy, 2.3% [n = 8]).

Data cutoff: January 31, 2023. [a]Percentages may not total 100 because of rounding. Shown are AE that occurred from the time of first dose of study treatment through 30 days after permanent discontinuation. AE were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03. [b]Grade 5 AE; none were considered treatment-related. AE, adverse event.

Courtesy of Neal D Shore, MD

Shore N et al. AUA 2023;Abstract LBA02-09.

Most common TEAEs

Most common TEAEs (>15% of patients), n (%)[a]	Enzalutamide combination (n = 353)		Leuprolide acetate (n = 354)		Enzalutamide monotherapy (n = 354)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Hot flash	243 (68.8)	2 (0.6)	203 (57.3)	3 (0.8)	77 (21.8)	1 (0.3)
Fatigue	151 (42.8)	12 (3.4)	116 (32.8)	5 (1.4)	165 (46.6)	14 (4.0)
Arthralgia	97 (27.5)	5 (1.4)	75 (21.2)	1 (0.3)	81 (22.9)	1 (0.3)
Hypertension	82 (23.2)	2 (0.6)	69 (19.5)	0	67 (18.9)	0
Fall	74 (21.0)	3 (0.8)	51 (14.4)	2 (0.6)	56 (15.8)	5 (1.4)
Back pain	60 (17.0)	1 (0.3)	54 (15.3)	0	62 (17.5)	1 (0.3)
Nausea	42 (11.9)	0	29 (8.2)	0	54 (15.3)	1 (0.3)
Gynecomastia	29 (8.2)	0	32 (9.0)	0	159 (44.9)	1 (0.3)
Nipple pain	11 (3.1)	0	4 (1.1)	0	54 (15.3)	0

- The most common AEs (>15% of patients) for all treatment cohorts were hot flash, fatigue; plus gynecomastia in the enzalutamide monotherapy cohort; most were grade <3.

Data cutoff: January 31, 2023. [a]Percentages may not total 100 because of rounding. Shown are AEs that occurred from the time of first dose of study treatment through 30 days after permanent discontinuation. AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03. TEAE, treatment-emergent AE.

Courtesy of Neal D Shore, MD

Shore N et al. AUA 2023;Abstract LBA02-09.

Selected TEAEs of special interest

Clustered TEAEs of special interest, n (%)[a]	Enzalutamide combination (n = 353)		Leuprolide acetate (n = 354)		Enzalutamide monotherapy (n = 354)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Fatigue[b]	178 (50.4)[c]	14 (4.0)	134 (37.9)[c]	6 (1.7)	191 (54.0)[c]	17 (4.8)
Musculoskeletal events[d]	163 (46.2)[c]	13 (3.7)	148 (41.8)[c]	4 (1.1)	158 (44.6)[c]	6 (1.7)
Hypertension	89 (25.2)[c]	27 (7.6)	74 (20.9)	21 (5.9)	77 (21.8)[c]	20 (5.6)
Fall	74 (21.0)	4 (1.1)	51 (14.4)	4 (1.1)	56 (15.8)	7 (2.0)
Fracture[e]	65 (18.4)	14 (4.0)	48 (13.6)	9 (2.5)	39 (11.0)	7 (2.0)
Cognitive and memory impairment	53 (15.0)[c]	2 (0.6)	23 (6.5)	2 (0.6)	50 (14.1)[c]	0
Loss of consciousness[f]	20 (5.7)	17 (4.8)	12 (3.4)	6 (1.7)	12 (3.4)	8 (2.3)
Ischemic heart disease	19 (5.4)	14 (4.0)	20 (5.6)	11 (3.1)	32 (9.0)	21 (5.9)
Other selected CV events[g]	18 (5.1)	13 (3.7)	17 (4.8)	10 (2.8)	13 (3.7)	8 (2.3)
Convulsion (seizure)	4 (1.1)	2 (0.6)	0	0	3 (0.8)	2 (0.6)

- The most common AEs of special interest for all treatment cohorts (≥10% of patients) were fatigue, fall, fracture, hypertension, and musculoskeletal events.

Data cutoff: January 31, 2023. [a]Percentages may not total 100 because of rounding. Shown are AEs that occurred from the time of first dose of study treatment through 30 days after permanent discontinuation. AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03. [b]Fatigue events included asthenia. [c]The most common (≥10% of patients) TEAEs. [d]Musculoskeletal events included back pain, arthralgia, myalgia, musculoskeletal pain, pain in extremity, musculoskeletal stiffness, muscular weakness, and muscle spasms. [e]Fractures excluded tooth fracture and fracture of the penis. [f]Loss of consciousness included syncope and presyncope. [g]Other selected CV events included hemorrhagic central nervous system vascular conditions, ischemic central nervous system vascular conditions, and cardiac failure. CV, cardiovascular.

Courtesy of Neal D Shore, MD

Shore N et al. AUA 2023;Abstract LBA02-09.

Agenda

INTRODUCTION: Interdisciplinary Management of Prostate Cancer

MODULE 1: Key Data Sets

MODULE 2: Faculty Survey

MODULE 3: Faculty Cases

Appendix

RTP
RESEARCH
TO PRACTICE

What is your preferred ADT for patients with localized disease?

 Dr Shore	Relugolix
 Dr Taplin	LHRH agonist
 Dr Concepcion	No preference
 Dr Gomella	No preference
 Dr Gupta	LHRH agonist or relugolix
 Dr Hafron	Start with degarelix and then add leuprolide
 Dr Morris	No preference
 Dr Plimack	No preference

ADT = androgen deprivation therapy

What is your preferred ADT for patients with PSA-only (M0) disease?

 Dr Shore	Relugolix
 Dr Taplin	LHRH agonist
 Dr Concepcion	No preference
 Dr Gomella	LHRH agonist
 Dr Gupta	LHRH agonist or relugolix
 Dr Hafron	I do not use ADT in this setting
 Dr Morris	LHRH agonist
 Dr Plimack	Relugolix

RTP RESEARCH TO PRACTICE

What is your preferred ADT for patients with metastatic castration-sensitive prostate cancer?

 Dr Shore	Relugolix
 Dr Taplin	LHRH agonist
 Dr Concepcion	No preference
 Dr Gomella	Degarelix
 Dr Gupta	LHRH agonist
 Dr Hafron	Start with degarelix and then add leuprolide
 Dr Morris	LHRH agonist
 Dr Plimack	No preference

RTP RESEARCH TO PRACTICE

What is your preferred ADT for patients with metastatic castration-sensitive prostate cancer and a history of coronary artery disease?

 Dr Shore	Relugolix
 Dr Taplin	Degarelix or relugolix
 Dr Concepcion	Relugolix
 Dr Gomella	Degarelix
 Dr Gupta	Relugolix
 Dr Hafron	Start with degarelix and then add leuprolide
 Dr Morris	No preference
 Dr Plimack	Relugolix

RTP
RESEARCH TO PRACTICE

Based on your personal clinical experience and knowledge of available data, what do you consider to be a relative or absolute contraindication to administering abiraterone?

	Relative contraindication	Absolute contraindication
 Dr Shore	Diabetes/cardiovascular issues	Diabetes/unstable CHF
 Dr Taplin	Liver disease	CHF
 Dr Concepcion	HTN, CHF, CAD, liver dysfunction	Uncontrolled HTN, cirrhosis
 Dr Gomella	High BP, liver issues	Liver failure
 Dr Gupta	Poorly controlled diabetes, obesity	Significant cardiac disease
 Dr Hafron	Cardiac, diabetes	None
 Dr Morris	Poorly controlled diabetes	None
 Dr Plimack	Diabetes	None

CHF = congestive heart failure; HTN = hypertension; CAD = coronary artery disease

What is the percent chance that a patient will experience toxicity during treatment with abiraterone that will require withholding dosing or discontinuation? What is the primary toxicity patients experience that leads to withholding dosing?

	Chance of holding or discontinuation	Primary toxicity
 Dr Shore	20%	Glycemia
 Dr Taplin	30%	HTN
 Dr Concepcion	<10%	HTN, elevated LFTs, hypokalemia
 Dr Gomella	50%	Edema, fatigue
 Dr Gupta	50%	Hepatotoxicity, cardiac toxicity, fatigue
 Dr Hafron	20%	Cardiac issues, worsening diabetes
 Dr Morris	10%	Fatigue
 Dr Plimack	20%	LFTs, edema

HTN = hypertension; LFT = liver function test

Based on your personal clinical experience and knowledge of available data, what do you consider to be a relative or absolute contraindication to administering enzalutamide?

	Relative contraindication	Absolute contraindication
 Dr Shore	Cognition	CVA syndromes
 Dr Taplin	Cognitive dysfunction	Seizure disorder
 Dr Concepcion	Uncontrolled HTN, neurological dysfunction	History of seizures, malignant HTN
 Dr Gomella	Advanced age, seizure history	Falls due to drug
 Dr Gupta	Old age	Neurological dysfunction
 Dr Hafron	Neurological	Seizures
 Dr Morris	Recent CVA/MI	Seizure DO
 Dr Plimack	Dementia	None

CVA = cerebral vascular accident (stroke); HTN = hypertension; MI = myocardial infarction

What is the percent chance that a patient will experience toxicity during treatment with enzalutamide that will require withholding dosing or discontinuation? What is the primary toxicity patients experience that leads to withholding dosing?

	Chance of holding or discontinuation	Primary toxicity
 Dr Shore	20%	Cognitive
 Dr Taplin	30%	HTN
 Dr Concepcion	<10%	Seizures, uncontrolled HTN
 Dr Gomella	25%	Cardiovascular events
 Dr Gupta	70%	Neurologic symptoms, myalgias, fatigue
 Dr Hafron	60%	Neurological
 Dr Morris	25%	Fatigue, mental fog
 Dr Plimack	20%	Fatigue

Based on your personal clinical experience and knowledge of available data, what do you consider to be a relative or absolute contraindication to administering apalutamide?

	Relative contraindication	Absolute contraindication
 Dr Shore	Cognition	CVA syndromes, skin hypersensitivities
 Dr Taplin	Uncontrolled HTN	None
 Dr Concepcion	Uncontrolled HTN, neurological dysfunction	History of seizures, malignant HTN
 Dr Gomella	Seizure, severe cardiovascular disease	Severe rash
 Dr Gupta	N/A	N/A
 Dr Hafron	Neurological	Seizures
 Dr Morris	Recent CVA, MI, significant rash DO	Seizure DO
 Dr Plimack	Need more experience and data	Need more experience and data

What is the percent chance that a patient will experience toxicity during treatment with apalutamide that will require withholding dosing or discontinuation? What is the primary toxicity patients experience that leads to withholding dosing?

	Chance of holding or discontinuation	Primary toxicity
 Dr Shore	20%	Rash
 Dr Taplin	20%	HTN
 Dr Concepcion	<10%	Seizures, uncontrolled HTN
 Dr Gomella	20%	Cardiovascular events
 Dr Gupta	40%	Severe rash, fatigue
 Dr Hafron	50%	Neurological, rash
 Dr Morris	10%	Fatigue
 Dr Plimack	Need more experience and data	Need more experience and data

Based on your personal clinical experience and knowledge of available data, what do you consider to be a relative or absolute contraindication to administering darolutamide?

	Relative contraindication	Absolute contraindication
 Dr Shore	None	None
 Dr Taplin	Uncontrolled HTN	None
 Dr Concepcion	Neurological dysfunction	Severe asthenia
 Dr Gomella	None usually	Cardiovascular events
 Dr Gupta	N/A	N/A
 Dr Hafron	None	Seizures
 Dr Morris	Recent CVA, MI, seizure DO	None
 Dr Plimack	Need more experience and data	Need more experience and data

What is the percent chance that a patient will experience toxicity during treatment with darolutamide that will require withholding dosing or discontinuation? What is the primary toxicity patients experience that leads to withholding dosing?

	Chance of holding or discontinuation	Primary toxicity
 Dr Shore	10%	Body aches
 Dr Taplin	10%	HTN
 Dr Concepcion	<10%	Asthenia
 Dr Gomella	10%	Cardiovascular events
 Dr Gupta	40%	Fatigue
 Dr Hafron	10%	Fatigue, increased LFTs, falls
 Dr Morris	5%	N/A
 Dr Plimack	Need more experience and data	Need more experience and data

For a patient with PSA-only (M0) prostate cancer for whom you are not able to access enzalutamide, would you consider substituting apalutamide or darolutamide, either with or without ADT, if you had access to both those agents?

 Dr Shore	Yes, either apalutamide or darolutamide
 Dr Taplin	Yes, either apalutamide or darolutamide
 Dr Concepcion	Yes, either apalutamide or darolutamide
 Dr Gomella	Yes, either apalutamide or darolutamide
 Dr Gupta	Yes, either apalutamide or darolutamide
 Dr Hafron	Yes, either apalutamide or darolutamide
 Dr Morris	Yes, either apalutamide or darolutamide
 Dr Plimack	Yes, either apalutamide or darolutamide

RTP
RESEARCH TO PRACTICE

For a patient with PSA-only (M0) prostate cancer for whom you are not able to access apalutamide would you consider substituting enzalutamide or darolutamide, either with or without ADT, if you had access to both of those agents?

 Dr Shore	Yes, darolutamide
 Dr Taplin	Yes, either darolutamide or enzalutamide
 Dr Concepcion	Yes, either darolutamide or enzalutamide
 Dr Gomella	Yes, either darolutamide or enzalutamide
 Dr Gupta	Yes, either darolutamide or enzalutamide
 Dr Hafron	Yes, either darolutamide or enzalutamide
 Dr Morris	Yes, darolutamide
 Dr Plimack	Yes, either darolutamide or enzalutamide

RTP RESEARCH TO PRACTICE

Based on your personal clinical experience and knowledge of available data, in general how would you compare the quality of life (QoL) for patients receiving intermittent ADT (eg, relugolix), intermittent ADT in combination with enzalutamide or intermittent enzalutamide alone?

 Dr Shore	Intermittent ADT has better QoL
 Dr Taplin	Intermittent ADT has better QoL
 Dr Concepcion	QoL is similar with all 3 regimens
 Dr Gomella	QoL is similar with all 3 regimens
 Dr Gupta	Intermittent ADT has better QoL
 Dr Hafron	QoL is similar with all 3 regimens
 Dr Morris	QoL is similar with all 3 regimens
 Dr Plimack	Intermittent ADT has better QoL

RTP RESEARCH TO PRACTICE

Based on your personal clinical experience and knowledge of available data, in general how would you compare the sexual function (libido/erectile function) of patients receiving intermittent ADT (eg, relugolix), intermittent ADT in combination with enzalutamide or intermittent enzalutamide alone?

 Dr Shore	Intermittent enzalutamide alone is associated with better sexual function
 Dr Taplin	Intermittent enzalutamide alone is associated with better sexual function
 Dr Concepcion	Sexual function is similar with all 3 regimens
 Dr Gomella	Intermittent ADT is associated with better sexual function
 Dr Gupta	Intermittent ADT is associated with better sexual function
 Dr Hafron	Sexual function is similar with all 3 regimens
 Dr Morris	Intermittent enzalutamide alone is associated with better sexual function
 Dr Plimack	Sexual function is similar with all 3 regimens

RTP RESEARCH TO PRACTICE

Based on your personal clinical experience and knowledge of available data, how problematic do you consider the gynecomastia in patients receiving androgen signal blocking agents without ADT?

 Dr Shore	Somewhat problematic
 Dr Taplin	Somewhat problematic
 Dr Concepcion	Somewhat problematic
 Dr Gomella	Not at all problematic
 Dr Gupta	Very problematic
 Dr Hafron	Very problematic
 Dr Morris	Somewhat problematic
 Dr Plimack	Very problematic

How effective is radiation therapy (RT) at treating or preventing gynecomastia (eg, 1 preemptive dose of low-dose RT)?

 Dr Shore	Very effective
 Dr Taplin	Not effective
 Dr Concepcion	Moderate
 Dr Gomella	Helpful but is rarely done today
 Dr Gupta	Somewhat
 Dr Hafron	It helps with pain in the breasts but does not prevent breast enlargement
 Dr Morris	Normally don't recommend, but if a patient is motivated it may be helpful
 Dr Plimack	I don't recommend this, it's not that effective after gynecomastia develops

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, do you think a patient with high-risk M0 disease who would generally be offered ADT should also be offered the opportunity to alternatively receive enzalutamide monotherapy?

 Dr Shore	Yes
 Dr Taplin	Yes
 Dr Concepcion	Yes
 Dr Gomella	No
 Dr Gupta	No
 Dr Hafron	No
 Dr Morris	Yes
 Dr Plimack	No

RTP
RESEARCH TO PRACTICE

Does your treatment approach differ for a patient with prostate cancer who experiences PSA-only relapse (M0) after primary local therapy and for whom conventional imaging is negative but PSMA PET is positive?

 Dr Shore	May discuss adding PARP inhibitor if HRR mutation
 Dr Taplin	Yes
 Dr Concepcion	Yes
 Dr Gomella	No
 Dr Gupta	Yes
 Dr Hafron	No
 Dr Morris	No
 Dr Plimack	No

HRR = homologous recombination repair

RTP RESEARCH TO PRACTICE

What are the most common sites of oligometastatic disease that you have observed in patients who experience PSA-only relapse (M0) after primary local therapy and for whom conventional imaging is negative but PSMA PET is positive?

 Dr Shore	Bone and lymph nodes
 Dr Taplin	Prostate bed, pelvic nodes, bone
 Dr Concepcion	Regional nodes
 Dr Gomella	Pelvic nodes followed by axial skeleton
 Dr Gupta	Bone and lymph nodes
 Dr Hafron	Soft tissue and bone
 Dr Morris	Small pelvic nodes (perirectal, iliac) isolated bony lesions in spine and ribs
 Dr Plimack	Lymph nodes

RTP RESEARCH TO PRACTICE

What forms of localized therapy have you used for patients with prostate cancer and oligometastatic disease?

 Dr Shore	SBRT
 Dr Taplin	SBRT, EBRT, ablation after RT with relapse in same area
 Dr Concepcion	Radiation therapy
 Dr Gomella	SBRT
 Dr Gupta	SBRT
 Dr Hafron	SABR, EBRT
 Dr Morris	SBRT primarily
 Dr Plimack	Radiation therapy

SBRT = stereotactic body radiation therapy; EBRT = external beam RT; SABR = stereotactic ablative RT

RTP RESEARCH TO PRACTICE

For a patient receiving RT for localized prostate cancer, in what clinical situations would you generally recommend adding concurrent endocrine therapy?

 Dr Shore	Grade Group (GG) 3-5
 Dr Taplin	For all except the most favorable (ie, low risk or very favorable intermediate risk [3 + 4, 1-2 cores])
 Dr Concepcion	N1 disease, HR/VHR
 Dr Gomella	Intermediate- and high-risk disease
 Dr Gupta	Rising PSA
 Dr Hafron	For NCCN unfavorable disease and higher
 Dr Morris	Intermediate risk short duration 6 mo, HR/VHR 18-24 mo
 Dr Plimack	Node-positive or PSA >40 ng/mL and high stage/grade

HR/VHR = high risk to very high risk

RTP RESEARCH TO PRACTICE

In general, when recommending endocrine therapy for a patient receiving RT for localized prostate cancer, what is your usual treatment? For how long do you generally continue the endocrine therapy (ET)?

	ET	Duration
 Dr Shore	GG3: ADT alone GG4, 5: ADT + abiraterone	18-24 months
 Dr Taplin	ADT alone	6 mo intermediate, HR 24 mo
 Dr Concepcion	ADT + abiraterone	2 years
 Dr Gomella	ADT + apalutamide	Indefinitely
 Dr Gupta	ADT + abiraterone	1-2 years
 Dr Hafron	ADT alone	4 mo intermediate, HR 18-24 mo
 Dr Morris	ADT +/- abiraterone	6 mo intermediate, HR/VHR 18-24 mo
 Dr Plimack	ADT + abiraterone	2 years

HR/VHR = high risk to very high risk

A patient with localized prostate cancer who received RT is now experiencing PSA-only progression with no evidence of metastatic disease (M0). PSMA scan is negative. In general, when recommending endocrine therapy in this setting, what is your usual treatment? For how long do you generally continue treatment?

	ET	Duration
 Dr Shore	ADT alone	9-12 months
 Dr Taplin	ADT alone	9 months
 Dr Concepcion	ADT + abiraterone	Indefinitely
 Dr Gomella	ADT + enzalutamide	Indefinitely
 Dr Gupta	ADT + apalutamide, enzalutamide or darolutamide	Until metastatic progression
 Dr Hafron	ADT	Intermittent
 Dr Morris	ADT +/- abiraterone	Induction 6 months, stop if PSA undetectable
 Dr Plimack	ADT alone	9 months then consider intermittent

A patient with prostate cancer s/p RP followed by RT for PSA-only relapse is now experiencing further PSA-only progression with no evidence of metastatic disease (M0). PSMA scan is negative. Regulatory and reimbursement issues aside, what do you consider to be the optimal endocrine treatment in this setting?

 Dr Shore	ADT + enzalutamide
 Dr Taplin	ADT alone
 Dr Concepcion	ADT + enzalutamide
 Dr Gomella	ADT + enzalutamide
 Dr Gupta	ADT alone
 Dr Hafron	ADT + enzalutamide
 Dr Morris	Discourage any ADT until documented metastasis; will likely change due to EMBARK
 Dr Plimack	ADT alone

RTP RESEARCH TO PRACTICE

A patient with prostate cancer s/p RP followed by RT for PSA-only relapse is now experiencing further PSA-only progression with no evidence of metastatic disease (M0). PSMA scan is negative. In general, do you use intermittent or continuous treatment when administering endocrine therapy in this setting? For how long do you typically continue the endocrine therapy?

	ET dosing	ET duration
 Dr Shore	Intermittent	8-12 months
 Dr Taplin	Intermittent	9 months
 Dr Concepcion	Continuous	6 months
 Dr Gomella	Continuous	Indefinitely
 Dr Gupta	Intermittent	Until progression or unacceptable toxicity
 Dr Hafron	Continuous	2 years
 Dr Morris	Intermittent	6 months
 Dr Plimack	Intermittent	9 months

A patient with prostate cancer s/p RP followed by RT for PSA-only relapse receives ADT alone for further PSA progression. He is now experiencing PSA progression with no evidence of metastatic disease (M0). PSMA scan is negative. Regulatory and reimbursement issues aside, what do you consider to be the optimal endocrine treatment in this setting?

 Dr Shore	Continue ADT and add enzalutamide
 Dr Taplin	Continue ADT alone
 Dr Concepcion	Continue ADT and add enzalutamide
 Dr Gomella	Continue ADT and add enzalutamide
 Dr Gupta	Continue ADT and add apalutamide, enzalutamide or darolutamide
 Dr Hafron	Continue ADT and add darolutamide
 Dr Morris	Continue ADT and add darolutamide
 Dr Plimack	Continue ADT alone or with abiraterone or other 2nd-generation androgen receptor inhibitor

RTP RESEARCH TO PRACTICE

A patient with prostate cancer s/p RP followed by RT for PSA-only relapse receives ADT alone for further PSA progression. He is now experiencing PSA progression with no evidence of metastatic disease (M0). PSMA scan is negative. In general, do you use intermittent or continuous treatment when administering endocrine therapy in this setting? For how long do you typically continue the endocrine therapy?

	ET dosing	ET duration
 Dr Shore	Continuous	Until radiographic progression
 Dr Taplin	Continuous	Indefinitely
 Dr Concepcion	Continuous	6 months
 Dr Gomella	Continuous	Indefinitely
 Dr Gupta	Intermittent	Until metastatic or significant PSA progression
 Dr Hafron	Continuous	Indefinitely
 Dr Morris	Continuous	Until metastatic progression on imaging
 Dr Plimack	Continuous	Until metastatic progression on imaging

A patient who underwent RP for high-risk localized disease and received no further treatment is found to have metastatic disease. Genetic testing is negative for HRR mutations. Regulatory and reimbursement issues aside, what systemic treatment would you most likely recommend if the disease were ...?

	Asymptomatic, low volume	Symptomatic
 Dr Shore	ADT + abiraterone, enzalutamide or apalutamide	ADT + abiraterone, enzalutamide or apalutamide
 Dr Taplin	ADT + abiraterone	ADT + docetaxel + darolutamide
 Dr Concepcion	ADT + enzalutamide	ADT + docetaxel + darolutamide
 Dr Gomella	ADT + enzalutamide	ADT + docetaxel + darolutamide
 Dr Gupta	ADT + apalutamide	ADT + docetaxel + abiraterone ADT + docetaxel + darolutamide
 Dr Hafron	ADT + abiraterone	ADT + docetaxel + darolutamide
 Dr Morris	ADT + apalutamide	ADT + docetaxel + darolutamide
 Dr Plimack	ADT + abiraterone	ADT + docetaxel + darolutamide

A patient who underwent RT for localized high-risk prostate cancer and received no further treatment is found to have metastatic disease. Genetic testing is negative for HRR mutations. Regulatory and reimbursement issues aside, what systemic treatment would you most likely recommend if the disease were ...?

	Asymptomatic, low volume	Symptomatic
 Dr Shore	ADT + secondary hormonal therapy +/- docetaxel	ADT + secondary hormonal therapy +/- docetaxel
 Dr Taplin	ADT + abiraterone	ADT + abiraterone
 Dr Concepcion	ADT + enzalutamide	ADT + docetaxel + darolutamide
 Dr Gomella	ADT + enzalutamide	ADT + docetaxel + darolutamide
 Dr Gupta	ADT + apalutamide	ADT + abiraterone, enzalutamide or apalutamide
 Dr Hafron	ADT + abiraterone	ADT + docetaxel + darolutamide
 Dr Morris	ADT + apalutamide	ADT + docetaxel + darolutamide
 Dr Plimack	ADT + abiraterone	ADT + docetaxel + darolutamide

Agenda

INTRODUCTION: Interdisciplinary Management of Prostate Cancer

MODULE 1: Key Data Sets

MODULE 2: Faculty Survey

MODULE 3: Faculty Cases

Appendix

RTP
RESEARCH
TO PRACTICE

Clinical case (Scenario 1)

- 65 years old with rising PSA 3.2 to 6.1 over 2 years. Testosterone 320 ng/dL. Normal DRE.
- MRI prostate: 26 mL prostate. Extracapsular extension and seminal vesicle invasion. PIRADS 5
- Biopsy demonstrated Gleason 4+3=7 in 6 of 12 cores

Case (Scenario 2)

- MRI shows 1.4 cm left pelvic sidewall lymph node.
- CT abd/pelvis with left sided hydronephrosis from bladder thickening at left ureteral junction. Left pelvic lymphadenopathy. Bone scan negative. PSMA PET confirms cT4N1 disease.
- DRE cT4
- No significant comorbidities.

Which therapy would you recommend with EBRT?

1. ADT alone
2. ADT with bicalutamide
3. ADT with abiraterone/prednisone

Clinical Case: BCR

- 70 yo WM 18 months post RP
- PSA 5.0, PSADT 6 months
- Conventional Imaging (CT/BS) negative
- MedHx: ECOG 0; +HTN/elevated lipids
- Genomic profiling not done

Clinical Case: BCR, continued

Initiate therapy:

a. ADT alone
b. ADT + APA
c. ADT + Enza
d. Monotx Enza
e. Wait till conventional imaging positive

Clinical Case: BCR, continued

Questions:

1: Role genomic molecular markers (Decipher®, Prolaris®, Onco*type* DX®)

2: Role genetic alteration testing (germline, somatic)

3: Role PSMA PET

4: Role metastasis directed therapy (RT vs excision), +/- T suppression

Agenda

INTRODUCTION: Interdisciplinary Management of Prostate Cancer

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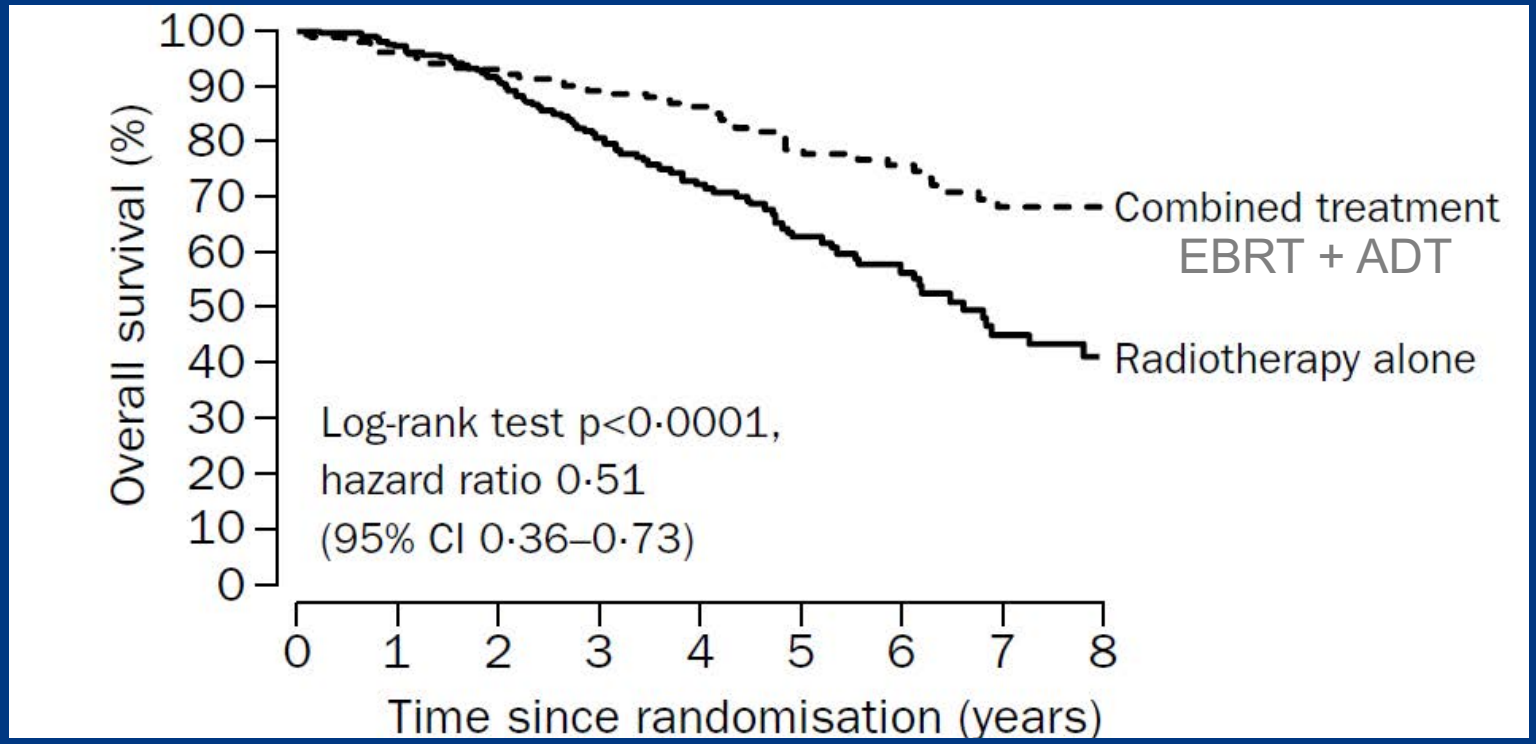
Appendix

RTP
RESEARCH
TO PRACTICE

ADT Is a Key Component of Treatment for High-Risk Prostate Cancer

Androgen deprivation therapy improves survival for men with high-risk prostate cancer when added to EBRT



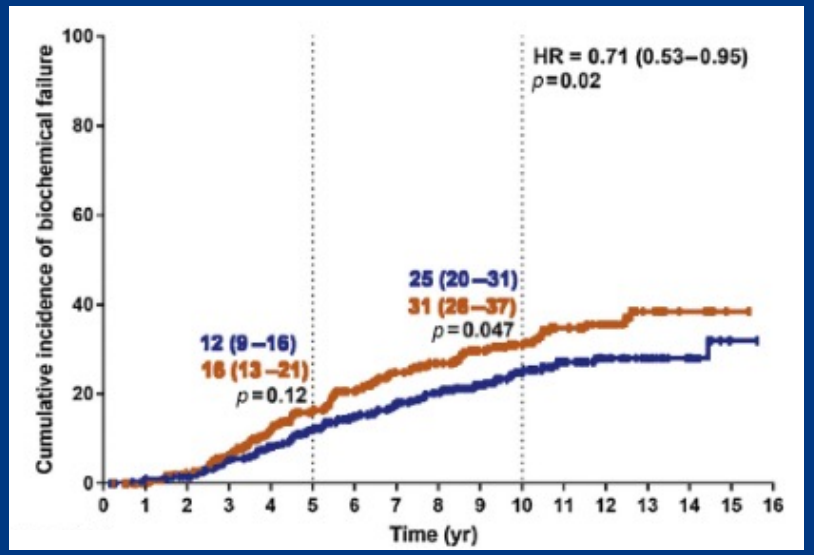
ADT Potentiates Radiation Damage by Blocking DNA Damage Repair

Courtesy of Neal D Shore, MD

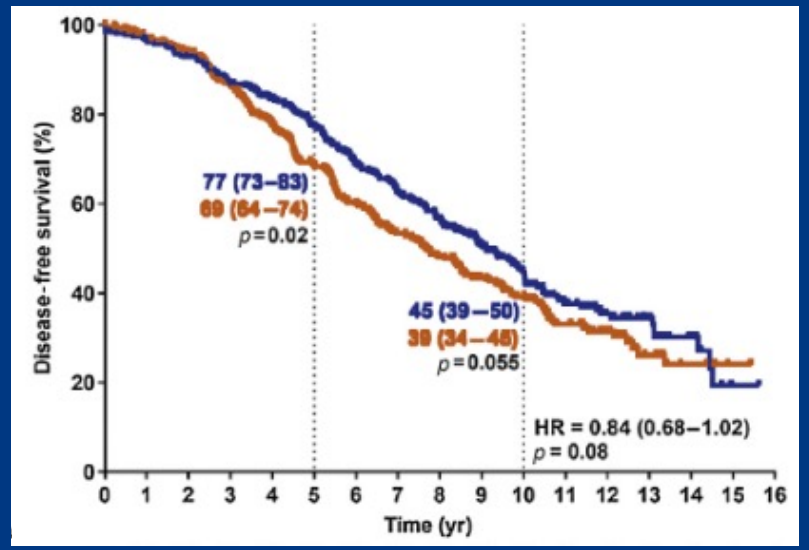
Bolla Lancet 2002. Goodwin JF Polkinghorn WR Cancer Discovery 2013.

18 Months of ADT Provides Better Quality of Life Than 36 months of ADT

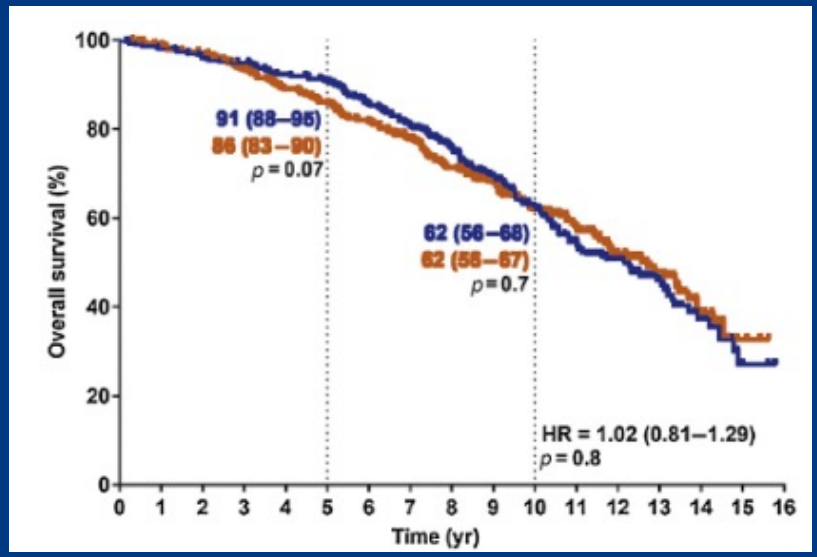
PCS IV, 2000-2008



More Frequent Biochemical Failure



No Difference Disease-specific survival



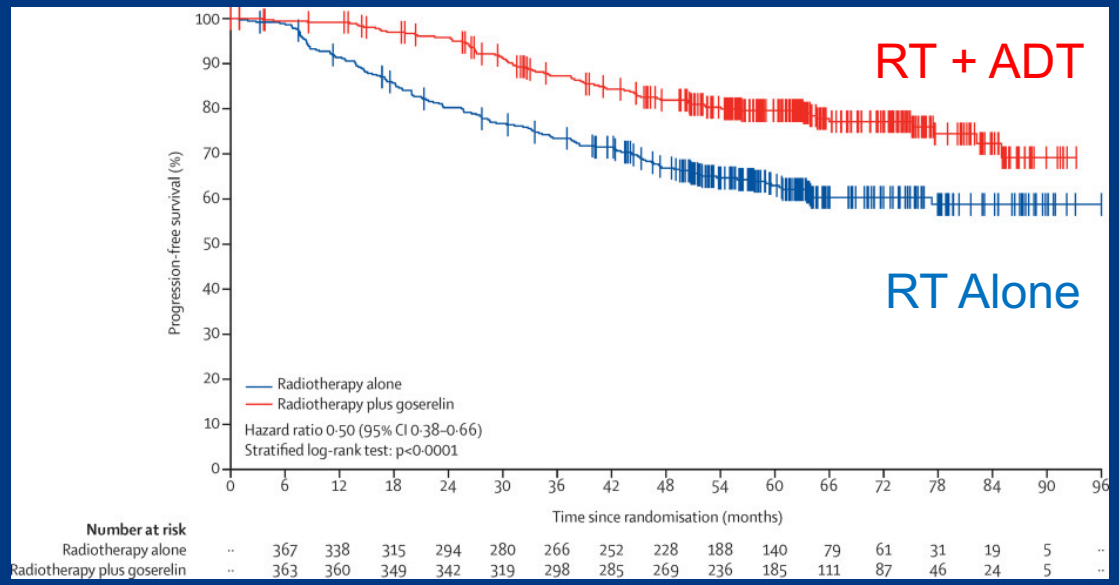
No Difference in OS BUT not a non-inferiority trial

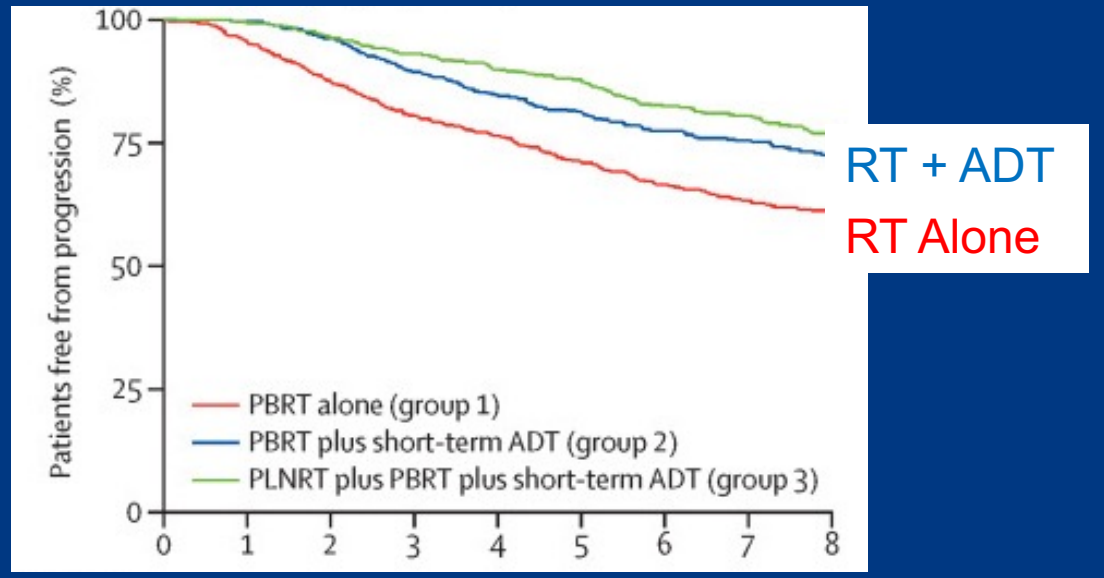
Courtesy of Neal D Shore, MD

Nabid A European Urology 2018; 74:432.

We Don’t Know The Optimal Choice

ADT is not required for all patients & may not be enough for some patients





GETUG 16

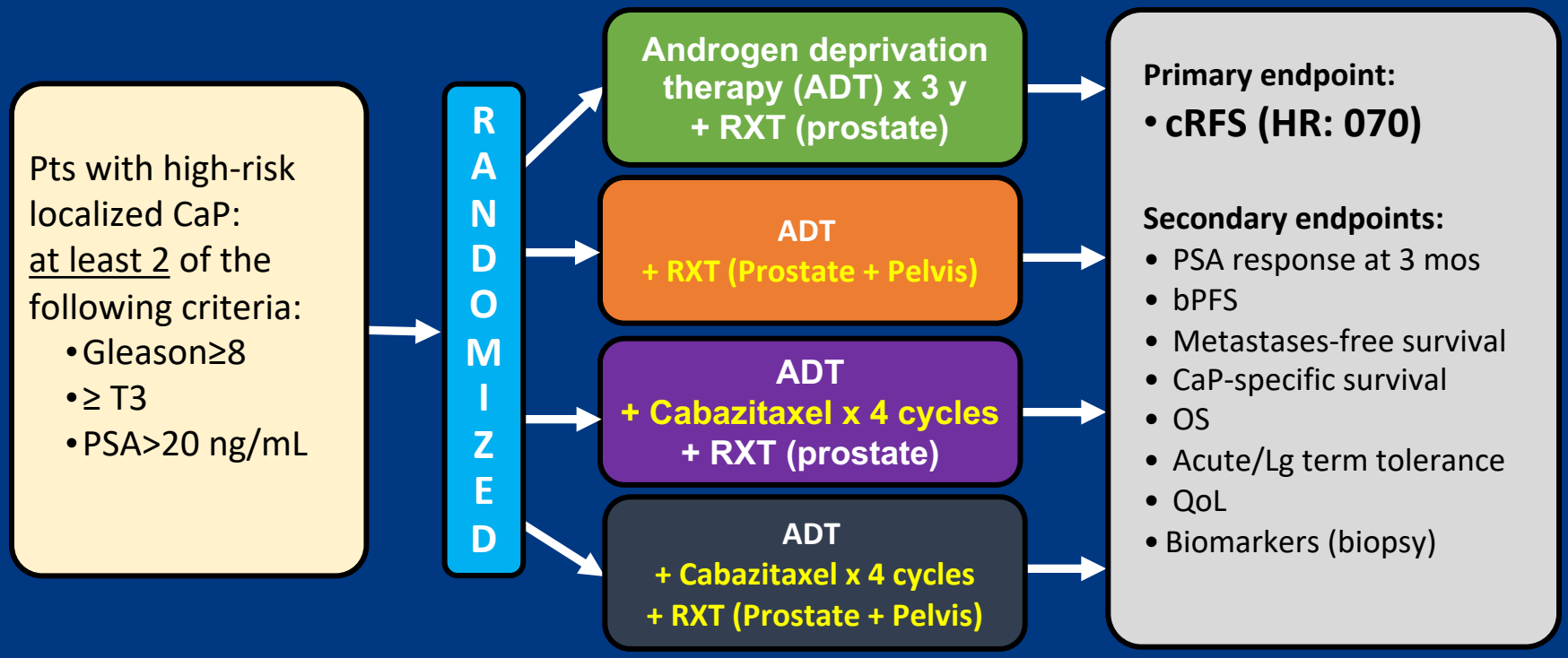
- 6 mo ADT improved freedom from progression
- **50% no recurrence** @10yrs w/ RT alone
- **29% recurred** @ 10 yrs w/ RT + ADT

SPPORT

- 4-6 mo ADT improved freedom from progression
- 70% no recurrence @5yrs w/ RT alone
- **20% recurred** @ 5 yrs w/ prostate bed RT + ADT

Courtesy of Neal D Shore, MD

PEACE-2: Phase III Trial of Cabazitaxel and Pelvic Irradiation in Patients With High-risk Localized Prostate Cancer



n= 750 pts (completed)

Study sponsor: Unicancer

NCT01952223

Courtesy of Neal D Shore, MD

STAMPEDE: Abiraterone ± Enzalutamide in nmCSPC

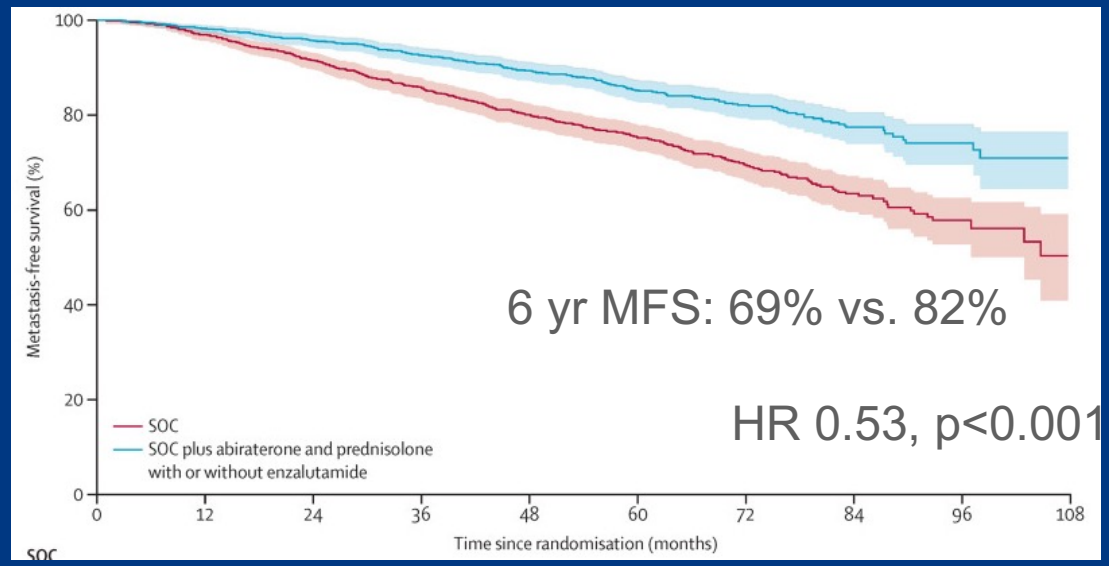
- Baseline characteristics well balanced
- Median age = 68
- Median PSA = 34
- 39% N1
- 79% Gleason 8-10
- 97% patients newly diagnosed
  - **85% receiving radiation**
  - **15% receiving primary ADT**
- Median follow-up = 72 months
- No benefit to abi + enza vs. abi alone
  - **arms combined**

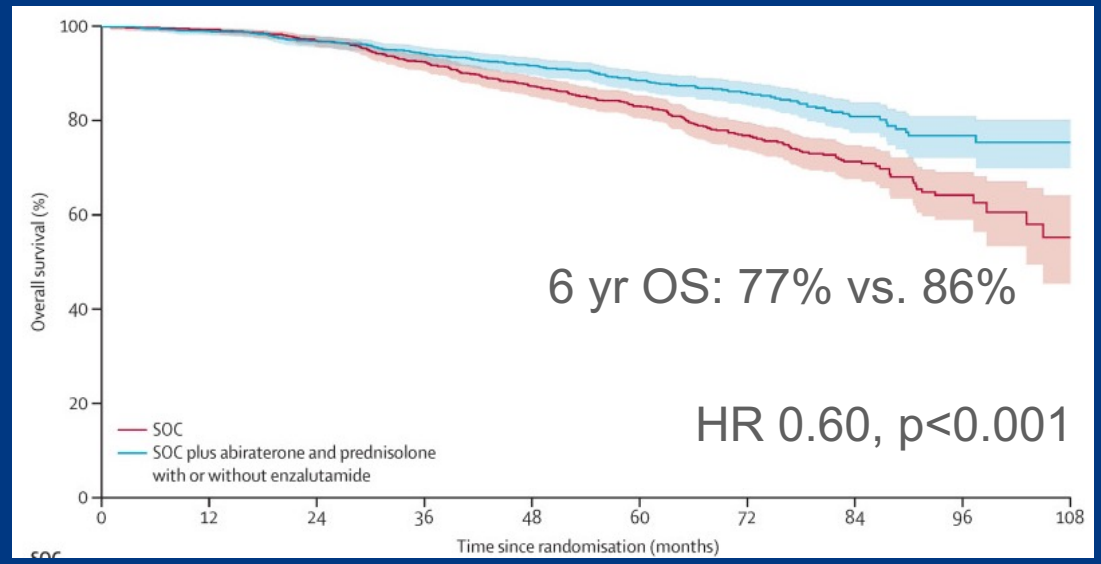
Courtesy of Neal D Shore, MD

Attard, et al. Lancet, 2022

Improvement in PFS, MFS, and OS with the Addition of Abiraterone and Prednisolone to ADT – Very High Risk

- STAMPEDE 1,974 PTS. Median 6-year follow up.
  - Node positive or 2 of the following: T3/4, Gleason 8-10, PSA >40, high-risk relapse





Metastasis-free survival	Overall survival

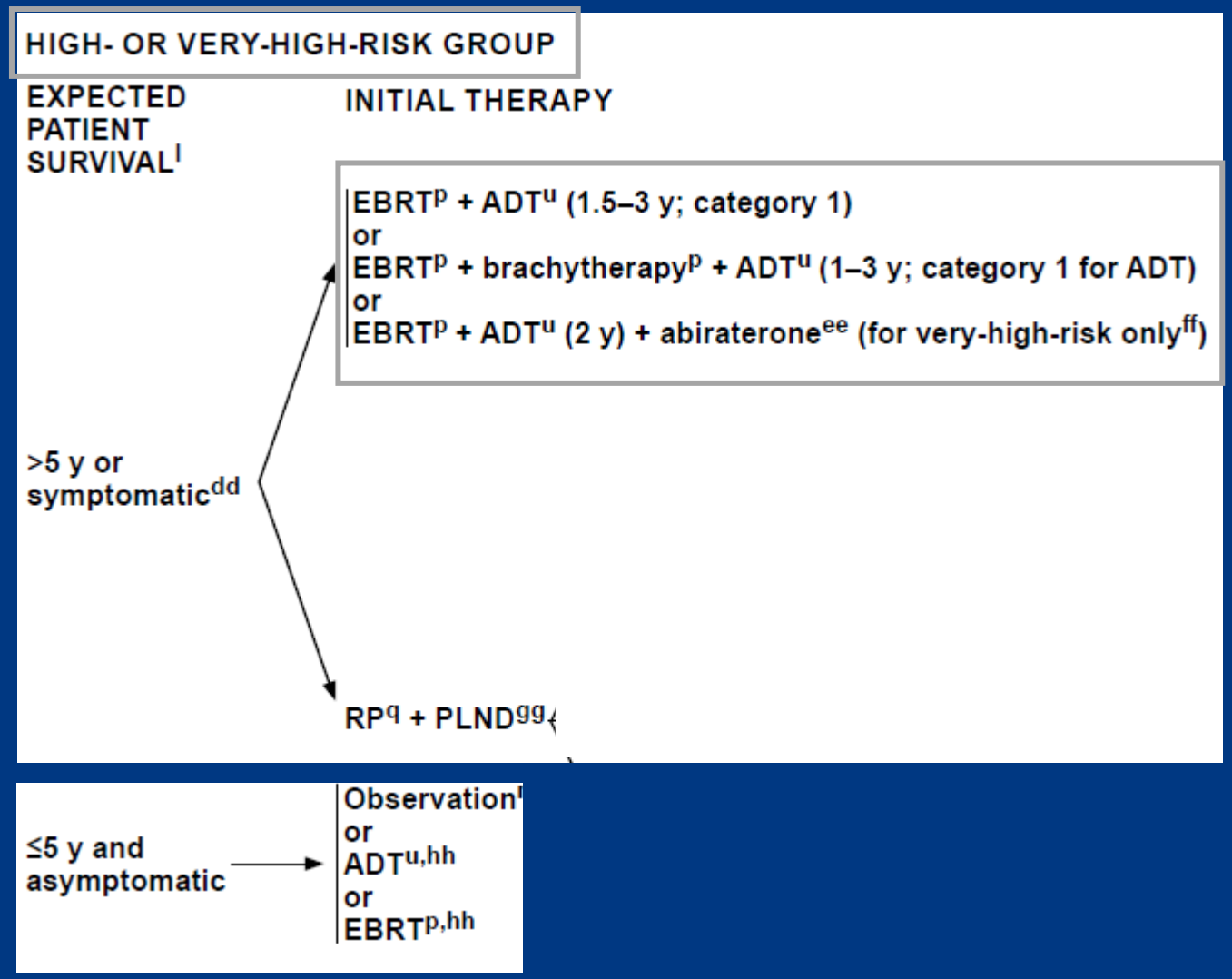
Median age 68. 73% T3/4. 79% GI8-10. Median PSA 34. 39% Node-positive

No additional benefit to enzalutamide in addition to abiraterone.

Courtesy of Neal D Shore, MD

Attard G Lancet 2021; 399:447.

Treatment Options For High-Risk Prostate Cancer



High-Risk

No very high-risk features and exactly one high-risk feature:

- cT3a OR
- Grade Group 4 or 5 OR
- PSA > 20 ng/ml

Very High-Risk

Has at least one of the following:

- cT3b to T4 OR
- Primary pattern 5 OR
- 2 to 3 high-risk features
- >4 cores with Grade Group 4 or 5

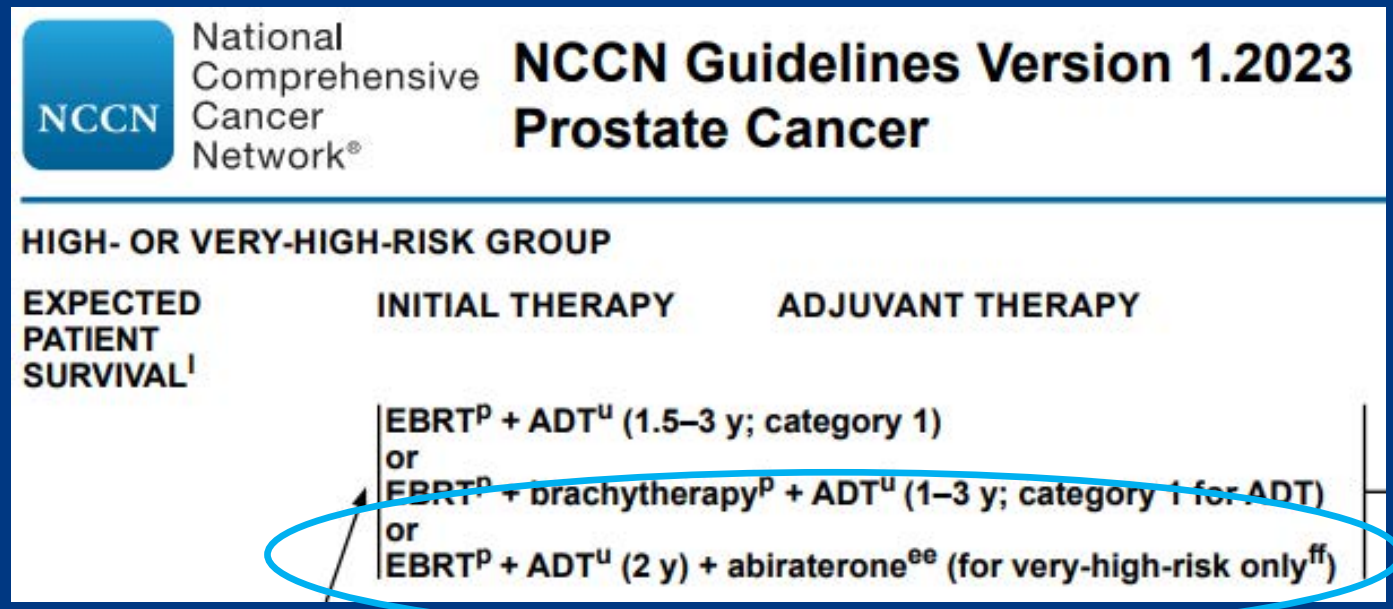
Courtesy of Neal D Shore, MD

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2023
Prostate Cancer

ADT with External Beam Radiation For Very High-Risk Prostate Cancer

- 24 months of ADT with abiraterone



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2023
Prostate Cancer

HIGH- OR VERY-HIGH-RISK GROUP

EXPECTED PATIENT SURVIVAL[l]	INITIAL THERAPY	ADJUVANT THERAPY
	EBRT[p] + ADT[u] (1.5–3 y; category 1)	
	or	
	EBRT[p] + brachytherapy[p] + ADT[u] (1–3 y; category 1 for ADT)	
	or	
	EBRT[p] + ADT[u] (2 y) + abiraterone[ee] (for very-high-risk only[ff])	

Very High-Risk
Has at least one of the following:
- cT3b to T4 OR
- Primary pattern 5 OR
- 2 to 3 high-risk features
- >4 cores with Grade Group 4 or 5

Courtesy of Neal D Shore, MD

Biochemically recurrent prostate cancer

- Men with biochemically recurrent prostate cancer following radical prostatectomy and a short PSA doubling time are at high risk for the development of distant metastases and prostate cancer related mortality[1]
- Intermittent androgen deprivation therapy (ADT) is a standard treatment approach for biochemically recurrent prostate cancer[2]
- A prior phase 3 study demonstrated non-inferiority of intermittent versus continuous ADT with respect to overall survival, with improvement in several key QOL parameters[3]

1. Pound CR, et al. JAMA 1999; 2. NCCN Guidelines version 4.2022; 3. Crook JM, et al. NEJM 2012

Courtesy of Neal D Shore, MD

Study Objectives

To compare each experimental arm versus control with respect to:

- Primary Objective: PSA progression-free survival, with PSA progression defined as **nadir + 2 ng/mL during treatment** or **> 0.2 ng/mL following treatment confirmed by repeat measurement (> 2 wks)**

- Secondary Objectives:
  - PSA progression-free survival in testosterone-evaluable population (T > 50 ng/dL)
  - Time to recovery of serum testosterone (T > 50 ng/dL)
  - Safety profile
  - 36-month PSA progression-free survival rate
  - Metastasis-free survival
  - Time to castration resistance
  - Short- and long-term patient reported quality of life

Courtesy of Neal D Shore, MD

Aggarwal R et al. ESMO 2022;Abstract LBA63.

Baseline Characteristics

	Arm A (N = 166)	Arm B (N = 168)	Arm C (N = 169)	Overall Study Cohort (N =503)
Median Age (Q1, Q3)	67.0 (60.3, 71.1)	66.0 (60.7, 70.3)	67.3 (62.4, 71.3)	66.7 (61.2, 70.9)
Race (%)				
American Indian/Alaska Native	1 (0.6)	0 (0.0)	2 (1.2)	3 (0.6)
Asian	3 (1.8)	0 (0.0)	10 (5.9)	13 (2.6)
Black or African-American	7 (4.2)	13 (7.7)	12 (7.1)	32 (6.4)
Native Hawaiian/Pacific Islander	1 (0.6)	0 (0.0)	1 (0.6)	2 (0.4)
Other	2 (1.2)	1 (0.6)	2 (1.2)	5 (1.0)
White	142 (85.5)	144 (85.7)	135 (79.9)	421 (83.7)
Unknown/Not Reported/Missing	10 (6.0)	10 (6.0)	7 (4.1)	27 (5.4)
Ethnicity (%)				
Hispanic	10 (6.0)	10 (6.0)	7 (4.1)	27 (5.4)
Non-Hispanic	151 (91.0)	152 (90.5)	155 (91.7)	458 (91.1)
Unknown/Not Reported/Missing	5 (3.0)	6 (3.6)	7 (4.1)	18 (3.6)

Courtesy of Neal D Shore, MD

Aggarwal R et al. ESMO 2022;Abstract LBA63.

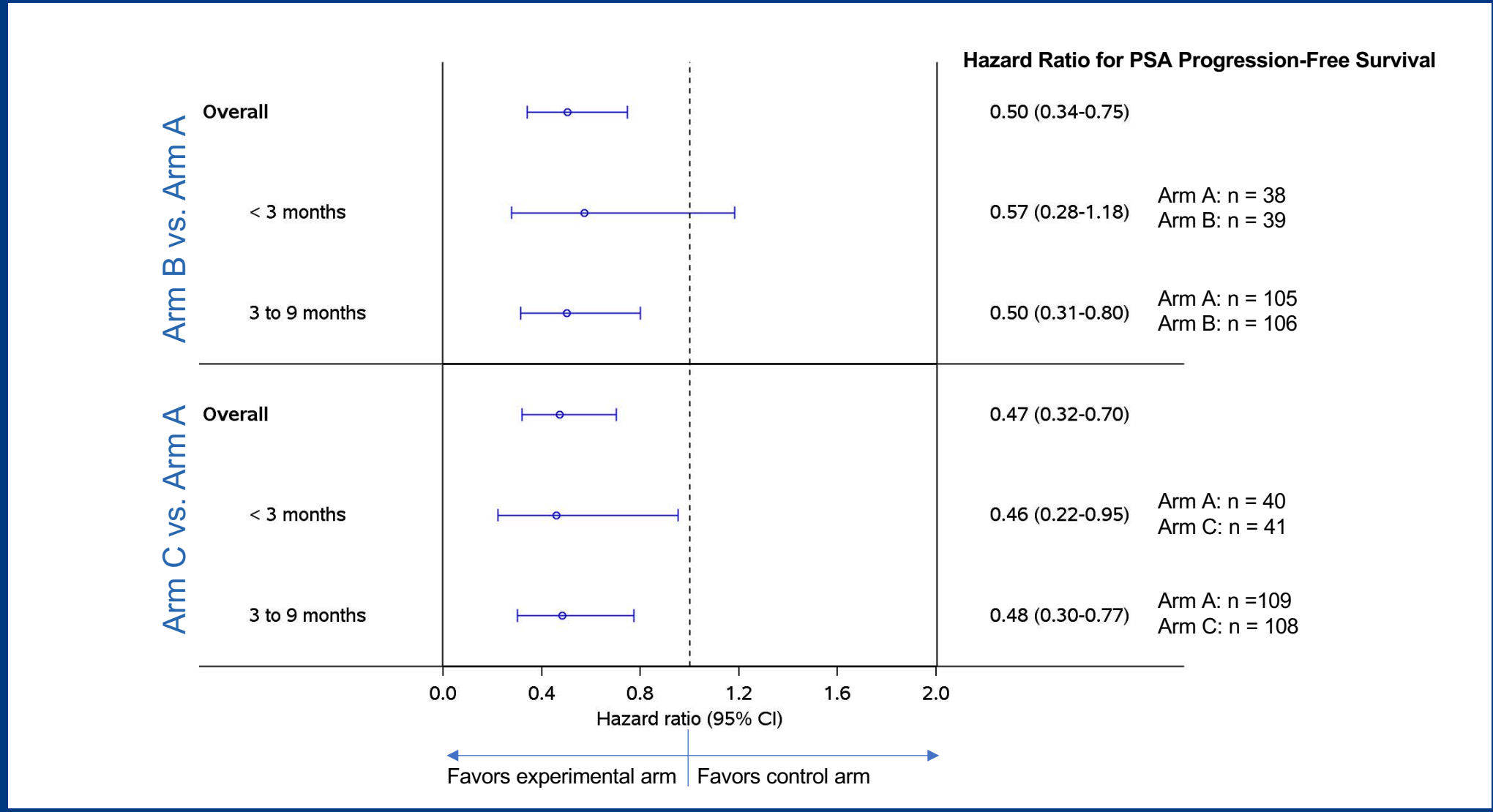
Baseline Characteristics, cont.

	Arm A (n = 166)	Arm B (n = 168)	Arm C (n = 169)	Overall Study Cohort (N = 503)
Median PSA at study entry, ng/mL (Q1, Q3)	1.73 (1.01, 3.20)	1.80 (0.97, 3.58)	1.77 (0.95, 4.21)	1.77 (0.97,3.57)
PSA doubling time strata (%)				
< 3 months	43 (25.9)	43 (25.6)	44 (26.0)	130 (25.8)
3 – 9 months	123 (74.1)	125 (74.4)	125 (74.0)	373 (74.2)
Median time interval between radical prostatectomy and study entry, years (Q1, Q3)	4.6 (2.8, 7.3)	4.7 (2.8, 6.5)	4.0 (2.8, 6.8)	4.4 (2.8, 6.8)
Prior radiation, N (%)	147 (88.6)	142 (84.5)	137 (81.1)	426 (84.7)
Prior androgen deprivation therapy, N (%)	71 (42.8)	75 (44.6)	67 (39.6)	213 (42.35)

Courtesy of Neal D Shore, MD

Aggarwal R et al. ESMO 2022;Abstract LBA63.

PSA Progression-Free Survival by PSA Doubling Time



Courtesy of Neal D Shore, MD

Aggarwal R et al. ESMO 2022;Abstract LBA63.

AUA 2023

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EMBARK: A Phase 3 Randomized Study of Enzalutamide or Placebo Plus Leuprolide Acetate and Enzalutamide Monotherapy in High-Risk Biochemically Recurrent Prostate Cancer

Neal D. Shore,[1] Murilo de Almeida Luz,[2] Ugo De Giorgi,[3] Martin Gleave,[4] Geoffrey T. Gotto,[5] Gabriel P. Haas,[6] Miguel Ramirez-Backhaus,[7] Antti Rannikko,[8] Jamal Tarazi,[9] Swetha Sridharan,[10] Jennifer Sugg,[6] Yiyun Tang,[11] Ronald F. Tutrone, Jr.,[12] Balaji Venugopal,[13] Arnauld Villers,[14] Henry H. Woo,[15] Fabian Zohren,[16] Stephen J. Freedland[17]

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ASCO Genitourinary Cancers Symposium

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ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

Introduction

- Within 10 years following definitive therapy, between 20–50% of patients experience disease recurrence characterized by rising PSA levels.[1-3]
- Limited level 1 clinical data exist for the treatment of patients with BCR.
- Patients with high-risk BCR are at increased risk of prostate cancer-specific mortality.[3-5]
- Evidence from phase 3 clinical trials demonstrates that treatment intensification with ARSI, such as enzalutamide, consistently improves patient outcomes across the prostate cancer continuum.[6-10]

The objective of EMBARK was to evaluate enzalutamide in combination with leuprolide acetate and enzalutamide monotherapy in patients with high-risk BCR.

1. Kupelian PA, et al. *Cancer.* 2002;95:2302–7. 2. Kupelian PA et al. *Urology*. 2006;68;593–8. 3. Freedland SJ et al. *JAMA*. 2005;294:433–9. 4. Freedland SJ, et al. *J Clin Oncol*. 2007; 25:1765–71. 5. Markowski MC, et al. *Clin Genitourin Cancer.* 2019;17:470–1. 6. Scher HI, et al. *N Engl J Med.* 2012;367:1187–97. 7. Beer TM, et al. *N Engl J Med.* 2014;371:424–33. 8. Hussain M, et al. *N Engl J Med*. 2018;378:2465–74. 9. Armstrong AJ, et al. *J Clin Oncol.* 2019;37:2974–86. 10. Davis ID, et al. *N Engl J Med.* 2019;381:121–31. ARSI, androgen receptor signaling inhibitor; BCR, biochemical recurrence; PSA, prostate-specific antigen.

Courtesy of Neal D Shore, MD

Shore N et al. AUA 2023;Abstract LBA02-09.

Demographics

Characteristic	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)	Enzalutamide monotherapy (n = 355)
Age, median (range), yr	69 (51–87)	70 (50–92)	69 (49–93)
Race, n (%)[a]			
White	293 (82.5)	301 (84.1)	295 (83.1)
Asian	26 (7.3)	26 (7.3)	26 (7.3)
Black	16 (4.5)	16 (4.5)	15 (4.2)
Other[b]	10 (2.8)	10 (2.8)	5 (1.4)
PSADT, n (%)[c]			
≤3 mo	69 (19.4)	80 (22.3)	76 (21.4)
>3 to ≤9 mo	285 (80.3)	277 (77.4)	278 (78.3)
PSADT, median, mo	4.6	5.0	5.0
Serum PSA, median, n (%), ng/mL[d]	5.0	5.5	5.3
≤10	278 (78.3)	273 (76.3)	272 (76.6)
>10	77 (21.7)	83 (23.2)	82 (23.1)
Prior hormonal therapy, n (%)	107 (30.1)	113 (31.6)	112 (31.5)
RP alone, n (%)	90 (25.4)	75 (20.9)	99 (27.9)
RT alone, n (%)	86 (24.2)	104 (29.1)	90 (25.4)
RP and RT, n (%)	179 (50.4)	179 (50.0)	166 (46.8)

[a]Not reported included: enzalutamide combination, n = 10 (2.8%); leuprolide acetate, n = 5 (1.4%); enzalutamide monotherapy, n = 14 (3.9%). [b]Includes patients who identified as multiple races (enzalutamide combination, n = 5; leuprolide acetate, n = 9; enzalutamide monotherapy, n = 5), American Indian or Alaskan Native (enzalutamide combination, n = 4; leuprolide acetate, n = 1; enzalutamide monotherapy, n = 0), Native Hawaiian or other Pacific Islander (enzalutamide combination, n = 1; leuprolide acetate and enzalutamide monotherapy, n = 0). [c]Missing included n = 1 (0.3%) for each treatment group. [d]Missing included: leuprolide acetate, n = 2; enzalutamide monotherapy, n = 1. RT, radiation therapy; yr, year.

Courtesy of Neal D Shore, MD

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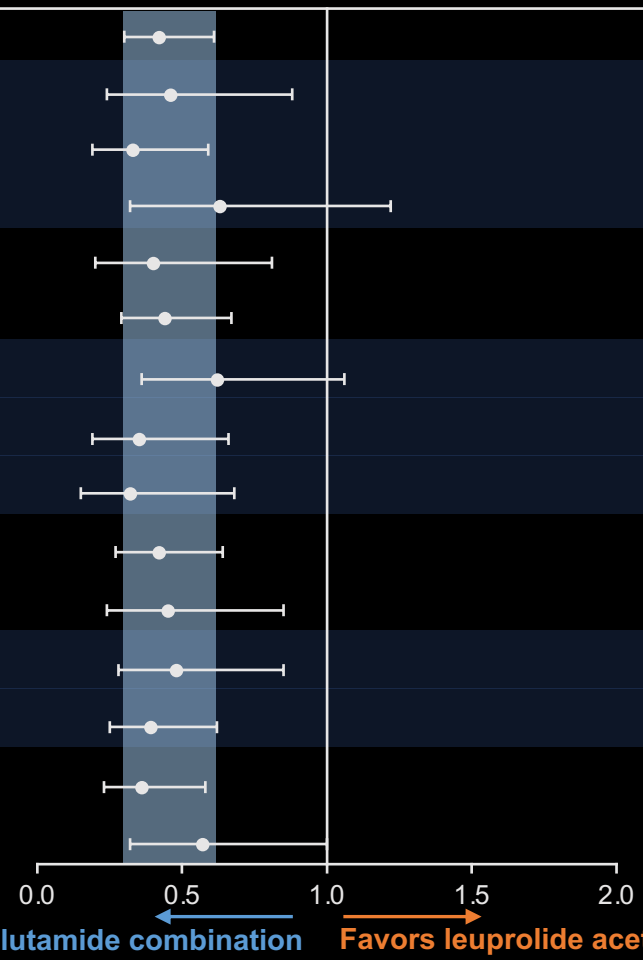
Subgroup analysis of MFS for enzalutamide combination vs. leuprolide acetate

Subgroup		Enzalutamide combination	Leuprolide acetate	MFS HR (95% CI)
		Events, n /patients, n		
All patients		45/355	92/358	0.42 (0.30–0.61)
PSADT	≤3 mo	14/69	30/80	0.46 (0.24–0.88)
	>3 to ≤6 mo	18/187	35/142	0.33 (0.19–0.59)
	>6 to ≤9 mo	13/98	27/135	0.63 (0.32–1.22)
Baseline age	≤65 years	11/81	28/91	0.40 (0.20–0.81)
	≥65 years	34/274	64/267	0.44 (0.29–0.67)
Geographic region	North America	22/144	32/137	0.62 (0.36–1.06)
	Europe	14/130	33/128	0.35 (0.19–0.66)
	ROW	9/81	27/93	0.32 (0.15–0.68)
Baseline PSA	≤10 ng/mL	31/278	64/273	0.42 (0.27–0.64)
	>10 ng/mL	14/77	28/83	0.45 (0.24–0.85)
Prior hormonal therapy	Yes	19/107	34/113	0.48 (0.28–0.85)
	No	26/248	58/245	0.39 (0.25–0.62)
Prior RP	Yes	26/269	61/254	0.36 (0.23–0.58)
	No	19/86	31/104	0.57 (0.32–1.00)

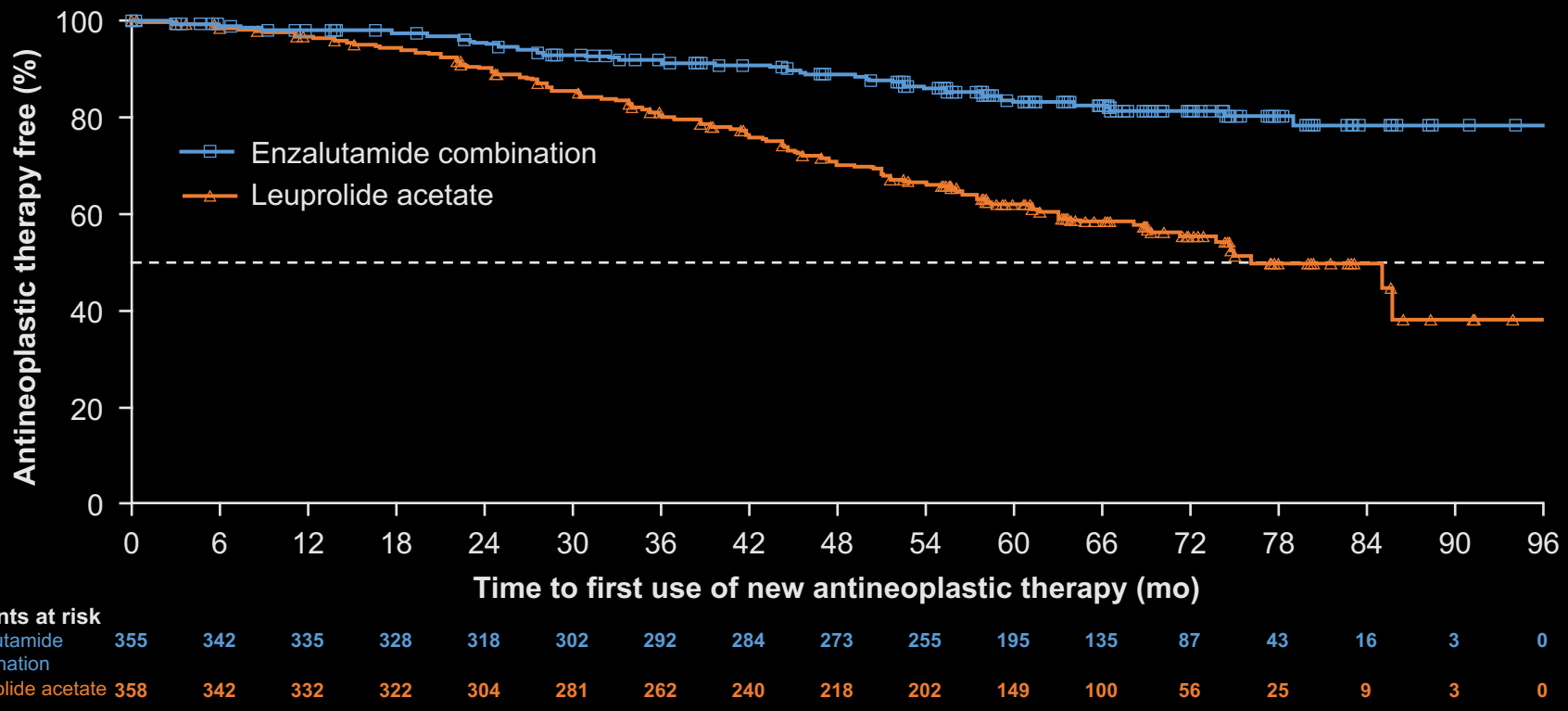


Data cutoff: January 31, 2023. For all patients, HR and 95% CI are based on stratified Cox regression model stratified by randomization stratification factors; for subgroups, HR and 95% CI are based on unstratified Cox regression model.

Courtesy of Neal D Shore, MD

Shore N et al. AUA 2023;Abstract LBA02-09.

Key secondary endpoint — Time to first use of new antineoplastic therapy for enzalutamide combination vs. leuprolide acetate



	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)
Events, n (%)	58 (16)	140 (39)
Median time to first use of new antineoplastic therapy (95% CI), mo	NR (NR)	76.2 (71.3–NR)

HR (95% CI): 0.36 (0.26–0.49); *P*<0.0001[a]

Data cutoff: January 31, 2023. Symbols indicate censored data. [a]The HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide combination; the two-sided *P*-value is based on a stratified log-rank test.

Courtesy of Neal D Shore, MD

Shore N et al. AUA 2023;Abstract LBA02-09.

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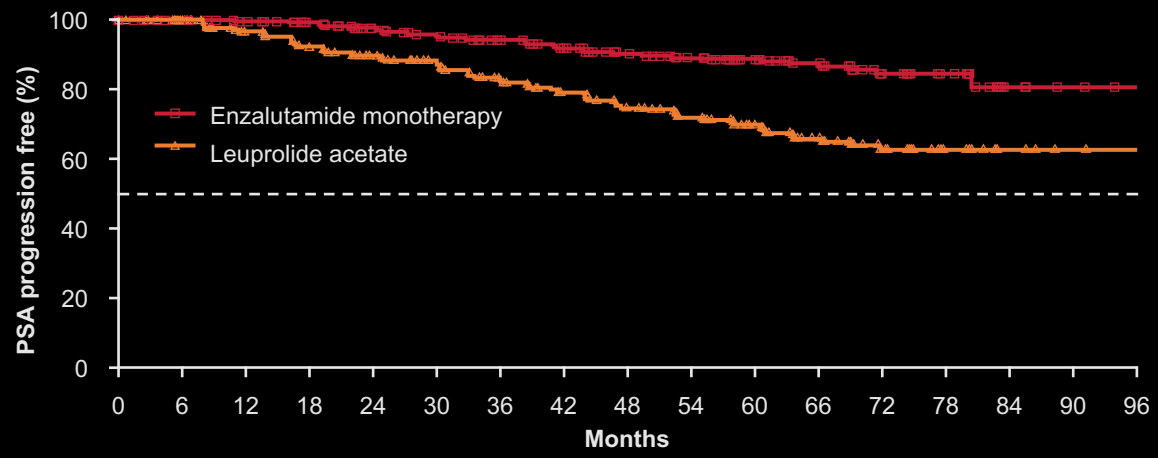
Key secondary endpoints — Enzalutamide monotherapy vs. leuprolide acetate

Time to PSA progression



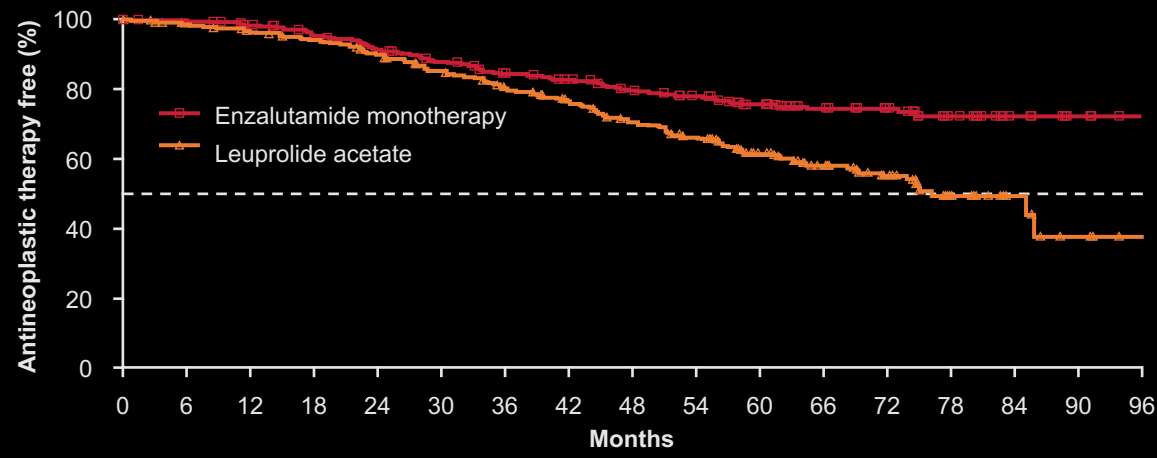
Patients at risk

Enzalutamide monotherapy	355	346	328	311	291	279	262	246	228	213	168	108	63	37	8	3	0
Leuprolide acetate	358	341	314	293	268	253	223	201	182	168	128	83	42	20	7	3	0

	Enzalutamide monotherapy (n = 355)	Leuprolide acetate (n = 358)
Events, n (%)	37 (10)	93 (26)
Median time to PSA progression (95% CI), mo	NR (NR)	NR (NR)

HR (95% CI): 0.33 (0.23–0.49); *P*<0.0001[a]

Time to first use of new antineoplastic therapy



Patients at risk

Enzalutamide monotherapy	355	352	341	327	312	297	279	268	252	240	192	124	80	40	12	3	0
Leuprolide acetate	358	342	332	322	304	281	262	240	218	202	149	100	56	25	9	3	0

	Enzalutamide monotherapy (n = 355)	Leuprolide acetate (n = 358)
Events, n (%)	84 (24)	140 (39)
Median time to first use of new antineoplastic therapy (95% CI), mo	NR (NR)	76.2 (71.3–NR)

HR (95% CI): 0.54 (0.41–0.71); *P*<0.0001[a]

Data cutoff: January 31, 2023. Symbols indicate censored data. [a]The HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide monotherapy; the two-sided *P*-value was based on a stratified log-rank test.

Courtesy of Neal D Shore, MD

Shore N et al. AUA 2023;Abstract LBA02-09.

EMBARK: Conclusions

- In patients with high-risk BCR, compared with leuprolide acetate, **enzalutamide combination** demonstrated a statistically significant and clinically meaningful improvement in MFS (HR 0.42; 95% CI, 0.30–0.61; *P*<0.0001).
  - A consistent treatment effect in pre-specified subgroups
  - Significant delays in time to PSA progression and time to first new antineoplastic therapy
  - A trend toward improved survival in interim analysis (HR 0.59; 95% CI, 0.38–0.90; *P*=0.0142); study ongoing for final analysis
- **Enzalutamide monotherapy** also demonstrated statistically significant and clinically meaningful improvements in MFS (HR 0.63; 95% CI 0.46–0.87; *P*=0.0049), time to PSA progression, and time to first new antineoplastic therapy.
  - A trend toward improved survival in interim analysis
- No new safety signals observed to date with enzalutamide treatment

Enzalutamide in combination with ADT, if approved in this setting, has the potential to become a new standard of care for patients with high-risk BCR.

Courtesy of Neal D Shore, MD

Shore N et al. AUA 2023;Abstract LBA02-09.

Inside the Issue: The Current and Future Role of CD20 x CD3 Bispecific Antibodies in the Management of Non-Hodgkin Lymphoma

A CME/MOC-Accredited Live Webinar

Wednesday, August 2, 2023
5:00 PM – 6:00 PM ET

Faculty

Martin Hutchings, MD, PhD
Loretta J Nastoupil, MD

Moderator

Neil Love, MD

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